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| (54) Title: NOVEL SULFONAMIDE COMPOUNDS AND USES THEREOF | | | |
| (57) Abstract | | | |
| <p>In accordance with the present invention, there is provided a novel class of sulfonamide compounds. Compounds of the invention contain a core sulfonamide group. Variable moieties connected to the sulfur atom and nitrogen atom of the sulfonamide group include substituted or unsubstituted hydrocarbyl moieties, substituted or unsubstituted heterocycle moieties, polycyclic moieties, halogen, alkoxy, ether, ester, amide, sulfonyl, sulfonamidyl, sulfide, carbamate, and the like. Invention compounds are capable of a wide variety of uses. For example sulfonamide compounds can act to modulate production of amyloid β protein and are useful in the prevention or treatment of a variety of diseases. Pharmaceutical compositions containing invention compounds are also provided. Such compositions have wide utility for the prevention or treatment of a variety of diseases.</p> | | | |

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NOVEL SULFONAMIDE COMPOUNDS AND USES THEREOF

FIELD OF INVENTION

5 The present invention relates to novel compounds which contain a sulfonamide moiety, and pharmaceutical compositions containing invention compounds. In addition, the present invention relates to therapeutic methods for the treatment and prevention of various disease conditions, especially Alzheimer's disease and other diseases relating to the deposition of amyloid.

BACKGROUND OF THE INVENTION

10 Alzheimer's disease (AD) is a progressive, neurodegenerative disease characterized by memory loss, language deterioration, impaired visuospatial skills, poor judgment, and indifferent attitude. It is the most common form of dementia, affecting nearly 50% of the elderly population over 85 years of age. There is currently no effective treatment to prevent the disease.

15 One of the major histopathological hallmarks of Alzheimer's disease is senile plaques which are found only in the brain, and especially in regions associated with memory, reasoning and cognition. The major constituent of senile plaques is amyloid β protein, an insoluble 40-42 amino acid polypeptide. Amyloid β protein is normally found in the plasma and cerebrospinal fluid of healthy individuals although its function is unknown. In the disease state increased production and/or reduced removal of amyloid β protein results in increases in protein levels in plasma and cerebrospinal fluid and
20 accumulation of the protein in the brain.

 Amyloid β protein is derived from amyloid precursor protein (APP) by proteolytic cleavage. Processing of APP to amyloid β protein and other APP cleavage fragments is governed by a group of enzymes termed secretases. One type of secretase, γ -secretase, is responsible for the protein cleavage that gives rise to amyloid β protein. Although the existence of a protein having the activity of γ -
25 secretase has been suggested, neither the gene encoding the protein, nor the protein itself has been completely isolated and characterized.

 Thus, there is a continuing need in the art for compounds that can specifically inhibit proteolytic cleavage of APP, thereby inhibiting amyloid β protein production. The present invention meets this and related needs by providing a family of novel compounds and related methods of use.

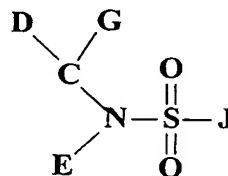
BRIEF DESCRIPTION OF THE INVENTION

In accordance with the present invention, we have discovered a class of sulfonamide compounds that inhibit amyloid β protein production. Compounds of the invention contain a core sulfonamide group. Variable moieties are connected to the sulfur atom and nitrogen atom of the sulfonamide group and include substituted or unsubstituted hydrocarbyl moieties, substituted or unsubstituted heterocyclic moieties, polycyclic moieties, halogen, alkoxy, ether, ester, amide, sulfonyl, sulfonamidyl, sulfide, and carbamate.

Invention compounds are capable of a wide variety of uses. For example, invention sulfonamide compounds can act to modulate amyloid β protein and are useful in the prevention and/or treatment of a variety of diseases. Without wishing to be bound by any theory, invention compounds are believed to act by blocking the proteolytic processing pathways that result in the formation of amyloid β proteins. Invention compounds are believed to act by inhibiting proteolytic cleavage of amyloid precursor protein (APP), the large precursor protein from which amyloid β protein is derived. Therapeutic indications for compounds with this inhibitory activity include disorders of the central nervous system in which amyloid β protein accumulates in the cerebral extracellular perivascular space, such as Alzheimer's disease. Pharmaceutical compositions containing invention compounds also have wide utility.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, there are provided compounds having the structure:



and pharmaceutically acceptable salts thereof, wherein:

D is hydrogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, halogen, alkoxy, ester, amide, or

D and G, taken together, form a substituted or unsubstituted cyclic moiety; and

E, is hydrogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, alkoxy, amide, sulfonyl, sulfonamidyl, sulfide or alkoxy; or

E and J, taken together, form a substituted or unsubstituted cyclic moiety; and

G, when not part of a cyclic moiety including D, is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, amine, amide, ester, ether or carbamate; and

5 J, when not part of a cyclic moiety including E, is substituted or unsubstituted hydrocarbyl, heterocycle optionally having one or more double bonds.

As employed herein, "hydrocarbyl" refers to straight chain, branched chain and cyclic (*i.e.*, ring-containing) monovalent and bivalent radicals derived from saturated or unsaturated moieties containing only carbon and hydrogen atoms. Straight and branched chain radicals have in the range of about 1 up
10 to 12 carbon atoms and cyclic hydrocarbyl radicals have in the range of about 3 up to about 20 carbon atoms. The term "substituted hydrocarbyl" refers to hydrocarbyl moieties further bearing substituents as set forth below.

Exemplary straight or branched chain hydrocarbyl moieties include alkyl moieties, alkenyl moieties, polyalkenyl (*e.g.*, dialkenyl moieties, and trialkenyl moieties), alkynyl moieties, alkadiynal moieties, alkatriynal moieties, alkenyne moieties, alkadienyne moieties, alkenediyne moieties, and the
15 like.

Exemplary cyclic hydrocarbyl moieties include cycloalkyl moieties, cycloalkenyl moieties, cycloalkadienyl moieties, cycloalkatrienyl moieties, cycloalkynyl moieties, cycloalkadiynyl moieties, aromatic moieties, spiro hydrocarbon moieties wherein two rings are joined by a single atom which is
20 the only common member of the two rings (*e.g.*, spiro[3.4]octanyl, and the like), bicyclic hydrocarbon moieties wherein two rings are joined and have at least two atoms in common (*e.g.*, bicyclo [3.2.1]octane, bicyclo [2.2.1]hept-2-ene, and the like), ring assemblies wherein two or more cyclic systems (*i.e.*, single rings or fused systems) are directly joined to each other by single or double bonds, and the number of such ring junctions is one less than the number of cyclic systems involved (*e.g.*,
25 biphenyl, biphenylene, radicals of *p*-terphenyl, cyclohexylbenzyl, and the like), polycyclic moieties, and the like;

"alkyl" refers to straight or branched chain alkyl radicals having in the range of about 1 up to 12 carbon atoms; "substituted alkyl" refers to alkyl radicals further bearing one or more substituents such as cycloalkyl, cycloalkenyl, aryl, heterocycle optionally having one or more double bonds, halogen, alkoxy,
30 cyano, cyanomethyl, nitro, amino, amide, amidine, hydroxy, carboxyl, carbamate, ether, ester, sulfonyl, sulfonamide, mercapto, and the like; "lower alkyl" refers to alkyl radicals having in the range of about 1 up to 6 carbon atoms; "substituted lower alkyl" refers to lower alkyl radicals further bearing one or more substituents as set forth above;

“alkenyl” refers to straight or branched chain hydrocarbyl radicals having at least one carbon-carbon double bond, and having in the range of about 2 up to 12 carbon atoms, and “substituted alkenyl” refers to alkenyl radicals further bearing one or more substituents as set forth above; “lower alkenyl” refers to alkenyl radicals having in the range of about 2 up to 6 carbon atoms; “substituted lower alkenyl” refers to lower alkenyl radicals further bearing one or more substituents as set forth above;

“alkynyl” refers to straight or branched chain hydrocarbyl radicals having at least one carbon-carbon triple bond, and having in the range of about 2 up to 12 carbon atoms, and “substituted alkynyl” refers to alkynyl radicals further bearing one or more substituents as set forth above;

“cycloalkyl” refers to ring-containing radicals containing in the range of about 3 up to 20 carbon atoms, and “substituted cycloalkyl” refers to cycloalkyl radicals further bearing one or more substituents as set forth above;

“cycloalkenyl” refers to ring-containing radicals having at least one carbon-carbon double bond in the ring, and having in the range of about 3 up to 20 carbon atoms, and “substituted cycloalkenyl” refers to cyclic alkenyl radicals further bearing one or more substituents as set forth above;

“cycloalkynyl” refers to ring-containing radicals having at least one carbon-carbon triple bond in the ring, and having in the range of about 7 up to 20 carbon atoms, and “substituted cycloalkynyl” refers to cyclic alkynyl radicals further bearing one or more substituents as set forth above;

“aromatic” refers to hydrocarbyl radicals having one or more polyunsaturated carbon rings having aromatic character, and having in the range of about 6 up to about 14 carbon atoms, and “substituted aromatic” refers to aromatic radicals further bearing one or more substituents as set forth above;

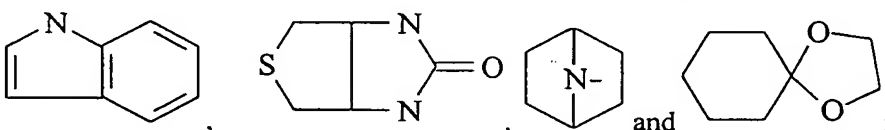
“aryl” refers to mononuclear aromatic radicals having 6 carbon atoms and fused ring aromatic radicals having up to about 14 carbon atoms, *i.e.* polynuclear aromatic radicals, and “substituted aryl” refers to aryl radicals further bearing one or more substituents as set forth above;

“alkylene” refers to divalent alkyl moieties wherein said moiety serves to link two structures together; “substituted alkylene” refers to alkylene moieties further bearing one or more substituents as set forth above;

“alkenylene”, refers to divalent alkenyl moieties wherein said moiety serves to link two structures together; “substituted alkenylene” refers to alkenylene moieties further bearing one or more substituents as set forth above;

“arylene” refers to divalent aryl moieties wherein said moiety serves to link two structures together; “substituted arylene” refers to arylene moieties further bearing one or more substituents as set forth above;

“heterocycle” refers to ring-containing monovalent and bivalent radicals having one or more heteroatoms (e.g., N, O, S) as part of the ring structure, and having in the range of 3 up to 20 atoms in the rings. Heterocyclic moieties may be saturated or unsaturated containing one or more double bonds, and may contain more than one ring. Heterocyclic moieties include, for example, monocyclic moieties such as piperazinyl, morpholinyl, thiomorpholinyl, imidazolyl, pyrimidinyl, isothiazolyl, isoxazolyl, pyrazinyl, pyrimidinyl, pyrazolyl, pyrrolyl, furanyl, pyranyl, thienyl, isoimidazolyl, triazolyl, dithiolyl, oxadithiolyl, isoxazolyl, oxazolyl, thiazolyl, isothiazolyl, pyronyl, dioxinyl, pyridinyl, pyridazinyl, triazinyl, oxazinyl, isoxazinyl, and the like, bicyclic heterocyclic moieties such as azabicycloalkanyl moieties, oxabicycloalkanyl moieties, and the like, spiro compounds containing heteroatoms, and ring assemblies containing heteroatoms. The term “substituted heterocycle” refers to heterocycles further bearing one or more substituents as set forth above. Exemplary radicals include radicals of polycyclic, bicyclic and spiro

heterocycles such as  ;

“halogen” refers to fluoride, chloride, bromide or iodide radicals;

“cyclic moiety” refers to substituted and unsubstituted cyclic hydrocarbyl moieties, as described above, and substituted and unsubstituted heterocycles, as described above;

“alkoxy” refers to radicals of the general formula -O-R, where R is substituted or unsubstituted hydrocarbyl; exemplary alkoxy radicals include methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, t-butoxy, and the like;

“ether” refers to radicals of the general formula -R'-O-R'', where R' and R'' are independently substituted or unsubstituted hydrocarbyl, or substituted or unsubstituted heterocycle optionally having one or more double bonds,

“ester” refers to radicals of the general formulae -C(O)O-R and -O-C(O)R, where R is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds; it is understood that the carbon atom of the ester group may be linked directly to the moiety of which ester is a substituent, or may be linked via a linker, such as substituted or unsubstituted alkylene, alkenylene, arylene, and the like;

“amine” refers to radicals of the general formula $-NRR'$, R and R' are independently hydrogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, alkoxy, ether, ester, amide. Thus, the radical may be a primary amine of the general formula, $-NH_2$, a secondary amine of the general formula $-NHR$, or a tertiary amine of the general formula $-NRR'$. It is understood that R and R' may cooperate to form a cyclic moiety having a nitrogen atom as a member of a ring; and that the nitrogen atom of the amine group may be linked directly to the moiety of which amine is a substituent, or may be linked via a linker, such as substituted or unsubstituted alkylene, alkenylene, arylene, and the like;

“amide” refers to radicals of the general formula $-C(O)NRR'$, wherein R and R' are independently hydrogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds; it is understood that R and R' may cooperate to form a cyclic moiety having a nitrogen atom as a member of a ring; and that the carbon atom of the amide group may be linked directly to the moiety of which amide is a substituent, or may be linked via a linker, such as substituted or unsubstituted alkylene, alkenylene, arylene, and the like;

“sulfide” refers to radicals of the general formula $-SR$, wherein R is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, ester, amine, amide, and the like;

“sulfonyl” refers to moieties containing a sulfonyl radical ($-SO_2-$);

“sulfonamidyl” refers to moieties containing a sulfonamide radical ($-SO_2-NRR'$), wherein R and R' are independently substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds; it is understood that R and R' may cooperate to form a cyclic moiety having a nitrogen atom as a member of a ring; and that the sulfur atom of the sulfonamide radical may be linked directly to the moiety of which amide is a substituent, or may be linked via a linker, such as substituted or unsubstituted alkylene, alkenylene, arylene, ether, ester, and the like;

“carbamate” refers to moieties containing a radical having the general formula $-O-C(O)-NRR'$ wherein R and R' are independently substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds; it is understood that R and R' may cooperate to form a cyclic moiety having a nitrogen atom as a member of a ring; and that the oxygen atom of the carbamate group may be linked directly to the moiety of which carbamate is a substituent, or may be linked via a linker, such as substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, ether, ester, and the like;

In accordance with the present invention, D is hydrogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, halogen, alkoxy,

ester or amide, or D and E, taken together, form a substituted or unsubstituted cyclic moiety. In accordance with one embodiment of the invention, D is substituted or unsubstituted hydrocarbyl. Moieties contemplated for use in this embodiment of the invention include those wherein D is hydrogen or substituted or unsubstituted lower alkyl, with hydrogen and unsubstituted lower alkyl preferred, and

5 hydrogen and unsubstituted methyl especially preferred.

Further in accordance with the present invention, E is selected from substituted or unsubstituted hydrocarbyl, heterocycle optionally having one or more double bonds, alkoxyl, amide, sulfonyl, sulfonamidyl or sulfide. Presently preferred compounds of the invention are those wherein E is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted

10 or unsubstituted cycloalkyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, substituted or unsubstituted polycyclic moiety, substituted or unsubstituted aryl, and the like. Especially preferred moieties include substituted or unsubstituted aryl; when E is substituted aryl, a mono-substituted or di-substituted aryl is preferred, and preferred substituents are halogen, ester, alkyl, sulfur-linked alkyl, NO₂, SO₂, and the like, with halogen especially preferred.

15 In accordance with the present invention, G is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, amine, amide, ester, ether or carbamate. Thus, G can be substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted cyclic moiety, ester, amide, carboxylate, and the like.

20 In one embodiment of the invention, G is substituted or unsubstituted alkyl, with substituted lower alkyl presently preferred. Presently preferred substituents are halogen and heterocycle optionally containing one or more double bonds such as imidazolyl, morpholinyl, pyrazolyl, pyrrolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, tetrazolyl, and 5-methyltetrazolyl, and the like. In another embodiment of the invention, G is substituted or unsubstituted alkenyl, with substituted lower alkenyl preferred. A presently preferred

25 substituent of lower alkenyl is halogen. In yet another embodiment of the invention, G is unsubstituted alkynyl, with lower unsubstituted alkynyl presently preferred. In still another embodiment of the invention, G is unsubstituted cycloalkyl.

In accordance with another embodiment of the invention, G is a substituted or unsubstituted cyclic moiety. Presently preferred cyclic moieties include substituted or unsubstituted naphthalenyl; when

30 substituted, preferred substituents are ether moieties, especially 1-piperidinyl propoxyl.

In accordance with still another embodiment of the invention, G is an ester, represented by the formula -C(O)-OR. In presently preferred embodiments of the invention, R is substituted or unsubstituted lower alkyl or substituted aryl.

In accordance with another embodiment of the invention, G is carboxylate.

In accordance with a further embodiment of the invention, G is substituted or unsubstituted aryl. When G is substituted aryl, presently preferred substituents are substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, halogen, amide, ester, hydroxy, sulfonamide, sulfonyl, ether, and radicals of the general formula $-O-(CH_2)_n-S-aryl$, wherein n is 1 to 6.

In accordance with the present invention, J is a moiety attached to the sulfur atom of a sulfonamide group. J is substituted or unsubstituted hydrocarbyl, heterocycle optionally having one or more double bonds, or J and E, taken together, form a substituted or unsubstituted cyclic moiety. Thus J can be substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocycle optionally having one or more double bonds, or J and E, taken together can form a substituted or unsubstituted polycyclic moiety or substituted or unsubstituted ring assembly.

In accordance with a particular embodiment of the invention, J is substituted or unsubstituted alkyl, with substituted or unsubstituted lower alkyl presently preferred. Substituents of alkyl presently preferred in this embodiment are substituted and unsubstituted aryl. In accordance with another embodiment of invention, J is substituted or unsubstituted alkenyl with substituted lower alkenyl preferred, and aryl a preferred substituent.

In accordance with still another embodiment of the invention, J is a substituted or unsubstituted polycyclic moiety. Thus J can be pentalene, indene, naphthalene, azulene, and the like. Moieties contemplated for use in this embodiment of the present invention include substituted or unsubstituted naphthalene; preferred substituents are secondary and tertiary amines.

In accordance with yet another embodiment of the invention, J is substituted or unsubstituted heterocycle optionally containing one or more double bonds. Moieties contemplated for use in this embodiment of the invention include those where J is isothiazolyl, thiazolyl, thiazinyl, thiazepinyl, and the like, with substituted thiazolyl preferred.

In still another embodiment of the invention, J is substituted or unsubstituted aryl. When J is substituted, preferred substituent moieties include alkyl, -O-alkyl, -S-alkyl, -S-aryl, halogen, nitro and trifluoromethyl.

In yet another embodiment of the invention, J cooperates with E to form a substituted or unsubstituted polycyclic moiety. Thus, J can be a fused moiety such as substituted or unsubstituted bicyclic, or a substituted or unsubstituted ring assembly. Moieties contemplated for use in this embodiment include substituted and unsubstituted naphthalenyl and substituted and unsubstituted biphenyl.

Those of skill in the art will recognize that multiple isomers exist for a single chemical formula; each of the possible isomeric forms of the various empirical formulae set forth herein are contemplated by the invention.

Those of skill in the art recognize that invention compounds may contain one or more chiral centers, and thus can exist as racemic mixtures as well as in individual enantiomeric forms. For many applications, it is preferred to carry out stereoselective syntheses and/or to subject the reaction product to appropriate purification steps so as to produce substantially optically pure materials. Suitable stereoselective synthetic procedures for producing optically pure materials are well known in the art, as are procedures for purifying racemic mixtures into optically pure fractions. Those of skill in the art will further recognize that invention compounds may exist in polymorphic forms wherein a compound is capable of crystallizing in different forms. Suitable methods for identifying and separating polymorphisms are known in the art.

In accordance with another embodiment of the present invention, there are provided pharmaceutical compositions comprising sulfonamide compounds as described above, in combination with pharmaceutically acceptable carriers. Optionally, invention compounds can be converted into non-toxic acid addition salts, depending on the substituents thereon. Thus, the above-described compounds (optionally in combination with pharmaceutically acceptable carriers) can be used in the manufacture of medicaments useful for the treatment of a variety of indications.

"Pharmaceutically acceptable salt" refers to a salt of the compound used for treatment which possesses the desired pharmacological activity and which is physiologically suitable. The salt can be formed with organic acids such as acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptanoate, glycerophosphate, heptanoate, hexanoate, 2-hydroxyethanesulfonate, lactate, malate, maleate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, oxalate, tartrate, toluenesulfonate, undecanoate, and the like. The salt can also be formed with inorganic acids such as sulfate, bisulfate, chlorate, perchlorate, hemisulfate, hydrochloride, hydrobromide, hydroiodide, and the like. In addition, the salt can be formed with a base salt, including ammonium salts, alkali metal salts such as sodium salts, potassium salts, and the like; alkaline earth metal salts such as calcium salts, magnesium salts, and the like; salts with organic bases such as dicyclohexylamine salts, *N*-methyl-*D*-glucamine, phenylethylamine, and the like; and salts with amino acids such as arginine, lysine, and the like.

Sulfonamide compounds as described above can be readily prepared using synthetic chemistry techniques known to those of skill in the art. See the Examples section herein for detailed description of numerous exemplary synthetic protocols.

In accordance with the present invention, a method of modulating the level of Amyloid Precursor Protein (APP) is provided. The method includes contacting APP with at least one sulfonamide compound according to the invention. As employed herein, the phrase “modulating the level of” refers to altered levels of protein so that the level is different as a result of employing the invention method when compared to the level without employing the invention method. Modulating the level of APP includes the suppression or augmentation of the level of any one of a number of APP proteins such as a full-length APP, APP proteins having deletions, additions or substitutions of amino acids, APP proteins that are fragments of full-length APP protein, soluble APP (s-APP), insoluble APP, and the like. Exemplary APP proteins include APP₇₇₀, APP₇₅₁, APP_{695wt}, APP_{670/671}, APP_{670/671/717}, sAPP, α -sAPP, β -sAPP, and the like.

A variety of APP proteins are found in neural and non-neural tissues. APP₇₇₀ and APP₇₅₁ are wild-type APPs of 770 and 751 amino acid residues, respectively, that are found in non-neural tissues. APP_{695wt} is an APP of 695 residues that is expressed in neurons. APP_{670/671} is human APP, 695 residues in length, that has mutations at codons 670 and 671 (Swedish double mutation). APP_{670/671/717} is similar to APP_{670/671} with an additional mutation at codon 717 (Phe for Val). sAPP is soluble APP, α -sAPP is α -secretase-cleaved soluble APP and β -sAPP is β -secretase-cleaved APP.

In accordance with another embodiment of the invention, there are provided methods of treating a wide variety of disease conditions, said method comprising administering to a patient in need thereof a therapeutically effective amount of at least one of the sulfonamide compounds described above.

APP is believed to be involved in numerous disease states. Therefore, modulating the level of APP also provides a variety of therapeutic applications, such as the treatment of amyloid angiopathy, cerebral amyloid angiopathy, systemic amyloidosis, Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis of the Dutch type, inclusion body myositis, Down's syndrome, and the like.

As used herein, “treating” refers to inhibiting or arresting the development of a disease, disorder or condition and/or causing the reduction, remission, or regression of the symptoms of a disease, disorder or condition. Those of skill in the art will understand that various methodologies and assays may be used to assess the development of a disease, disorder or condition, and similarly, various methodologies and assays may be used to assess the reduction, remission or regression of a disease, disorder or condition.

As used herein, “administering” refers to means for providing sulfonamide compounds and/or salts thereof, optionally employing pharmaceutically acceptable carriers, as described herein, to a patient, using any suitable method of delivery, e.g., oral, sublingual intravenous, subcutaneous, transcutaneous,

intramuscular, intracutaneous, intrathecal, epidural, intraocular, intracranial, inhalation, rectal, vaginal, and the like administration. Administration in the form of creams, lotions, tablets, capsules, pellets, dispersible powders, granules, suppositories, syrups, elixirs, lozenges, injectable solutions, sterile aqueous or non-aqueous solutions, suspensions or emulsions, patches, and the like, is also contemplated. The active ingredients may be compounded with non-toxic, pharmaceutically acceptable carriers including, glucose, lactose, gum acacia, gelatin, mannitol, starch paste, magnesium trisilicate, talc, corn starch, keratin, colloidal silica, potato starch, urea, dextrans, and the like.

“Contacting” as employed herein may include administering in solution or in solid phase.

For purposes of oral administration, tablets, capsules, troches, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, or syrups, elixirs and lozenges containing various excipients such as calcium carbonate, lactose, calcium phosphate, sodium phosphate, and the like may be employed along with various granulating and disintegrating agents such as corn starch, potato starch, alginic acid, and the like, together with binding agents such as gum tragacanth, corn starch, gelatin, acacia, and the like. Lubricating agents such as magnesium stearate, stearic acid, talc, and the like may also be added. Preparations intended for oral use may be prepared according to any methods known to the art for the manufacture of pharmaceutical preparations and such preparations may contain one or more agents selected from the group consisting of a sweetening agent such as sucrose, lactose, saccharin, and the like, flavoring agents such as peppermint, oil of wintergreen, and the like, coloring agents and preserving agents in order to provide pharmaceutically palatable preparations. Preparations for oral use may also contain suitable carriers include emulsions, solutions, suspensions, syrups, and the like, optionally containing additives such as wetting agents, emulsifying and suspending agents, sweetening, flavoring and perfuming agents, and the like. Tablets may be uncoated or they may be coated by known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period of time.

For the preparation of oral liquids, suitable carriers include emulsions, solutions, suspensions, syrups, and the like, optionally containing additives such as wetting agents, emulsifying and suspending agents, sweetening, flavoring and perfuming agents, and the like.

For the preparation of fluids for parenteral administration, suitable carriers include sterile aqueous or non-aqueous solutions, suspensions, or emulsions. For parenteral administration, solutions for the practice of the invention may comprise sterile aqueous saline solutions, or the corresponding water soluble pharmaceutically acceptable metal salts, as previously described. For parenteral administration, solutions of the compounds used in the practice of the invention may also comprise non-aqueous solutions, suspensions, emulsions, and the like. Examples of non-aqueous solvents or vehicles are propylene glycol, polyethylene glycol, vegetable oils, such as olive oil and corn oil, gelatin, and injectable

organic esters such as ethyl oleate, and the like. Such dosage forms may also contain adjuvants such as preserving, wetting, emulsifying, and dispersing agents. They may be sterilized, for example, by filtration through a bacteria-retaining filter, by incorporating sterilizing agents into the compositions, by irradiating the compositions, or by heating the compositions. They can also be manufactured in the form of sterile
5 water, or some other sterile injectable medium immediately before use.

Aqueous solutions may also be suitable for intravenous, intramuscular, intrathecal, subcutaneous, and intraperitoneal injection. The sterile aqueous media employed are all readily obtainable by standard techniques well known to those skilled in the art. They may be sterilized, for example, by filtration through a bacteria-retaining filter, by incorporating sterilizing agents into the
10 compositions, by irradiating the compositions, by heating the compositions, and the like. They can also be manufactured in the form of sterile water, or some other sterile medium capable of injection immediately before use.

Compounds contemplated for use in the practice of the present invention may also be administered in the form of suppositories for rectal or vaginal administration. These compositions may be prepared by
15 mixing the drug with a suitable non-irritating excipient, such as cocoa butter, synthetic glyceride esters of polyethylene glycols, and the like, such materials being solid at ambient temperatures but liquify and/or dissolve in internal cavities to release the drug.

The preferred therapeutic compositions for inocula and dosage will vary with the clinical indication. Some variation in dosage will necessarily occur depending upon the condition of the patient being treated, and the physician will, in any event, determine the appropriate dose for the individual
20 patient. The effective amount of compound per unit dose depends, among other things, on the body weight, physiology, and chosen inoculation regimen. A unit dose of compound refers to the weight of compound without the weight of carrier (when carrier is used).

The route of delivery compounds and compositions used for the practice of the invention is
25 determined by the disease and the site where treatment is required. Since the pharmacokinetics and pharmacodynamics of the compounds and compositions described herein will vary somewhat, the most preferred method for achieving a therapeutic concentration in a tissue is to gradually escalate the dosage and monitor the clinical effects. The initial dose, for such an escalating dosage regimen of therapy, will depend upon the route of administration.

30 In accordance with invention methods, the medicinal preparation can be introduced parenterally, by dermal application, and the like, in any medicinal form or composition. It is used as a solitary agent of medication or in combination with other medicinal preparations. Single and multiple therapeutic dosage regimens may prove useful in therapeutic protocols.

As employed herein, the phrase "a therapeutically effective amount", when used in reference to invention methods employing sulfonamide compounds and pharmaceutically acceptable salts thereof, refers to a dose of compound sufficient to provide circulating concentrations high enough to impart a beneficial effect on the recipient thereof. The specific therapeutically effective dose level for any particular patient will depend upon a variety of factors including the disorder being treated, the severity of the disorder, the activity of the specific compound used, the route of administration, the rate of clearance of the specific compound, the duration of treatment, the drugs used in combination or coincident with the specific compound, the age, body weight, sex, diet and general health of the patient, and like factors well known in the medical arts and sciences. Dosage levels typically fall in the range of about 0.001 up to 100 mg/kg/day; with levels in the range of about 0.05 up to 10 mg/kg/day being preferred.

In still another embodiment of the invention, there are provided methods for preventing disease conditions in a subject at risk thereof, said method comprising administering to said subject a therapeutically effective amount of at least one of the sulfonamide compounds described above.

As used herein, the phrase "preventing disease conditions" refers to preventing a disease, disorder or condition from occurring in a subject who may be at risk for the disease, but has not yet presented any symptoms thereof. Those of skill in the art will understand that a variety of methods may be used to determine a subject at risk for a disease, and that whether a subject is at risk for a disease will depend on a variety of factors known to those of skill in the art, including genetic make-up of the subject, age, body weight, sex, diet, general physical and mental health, occupation, exposure to environmental conditions, marital status, and the like, of the subject.

"Subject in need thereof" is intended to mean a mammal, e.g., humans, domestic animals and livestock, having or at risk of having one or more diseases associated with a modified level of APP.

Those of skill in the art can readily identify a variety of assays that can be used to assess the activity of sulfonamide compounds of the invention. For example, one can use *in vitro* cell-based assays to assess amyloid β protein production in cells that are exposed to invention compounds compared to cells exposed to control conditions. For such assays, transfected cells that stably express various forms of APP and from which amyloid β protein is secreted are used. Methods to measure amyloid β protein, such as immunoprecipitation, enzyme-linked immunosorbant assay (ELISA) and radioimmunoassay, and the like are known in the art. Immunoprecipitation methodology can be used to detect radiolabeled amyloid β protein derived from transfected cells having ^{35}S -methionine-labeled APP (Haass *et al.*, (1992) *Nature*, 359:322-325 and Shoji *et al.* (1992) *Science*, 258:126-129). ELISA can be used to detect unlabeled amyloid β protein (Seubert *et al.* (1992) *Nature*, 359:325-327).

The invention will now be described in greater detail by reference to the following non-limiting examples.

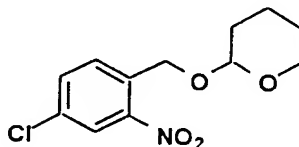
EXAMPLE 1

(S)-5-[[dimethyl(1,1-dimethylethyl)silyl]oxy]-1-pentanol

5 To a stirred solution of (4S)-pentane-1,4-diol [CAS 24347-57-7] (21.0 g, 0.202 mol) and *t*-butyldimethylsilyl chloride (30.5 g, 0.202 mol) in CH₂Cl₂ (400 mL) was added triethylamine (43.0 mL, 0.305 mol) followed by 4-(dimethylamino)pyridine (2.50 g, 20.2 mmol) at 0 °C. The mixture was stirred for 3 h at 0 °C and was diluted with diethyl ether (300 mL). The white precipitate was filtered and washed with diethyl ether. The filtrate was concentrated under reduced pressure. The pale yellow
10 oil was distilled (100 °C-103 °C at 0.7 mm) to afford the title compound (41 g, 92%) as a colorless oil. ¹H NMR (CDCl₃) δ 3.81 (m, 1H), 3.65 (m, 2H), 1.48-1.63 (m, 4H), 1.19 (d, 3H), 0.91 (s, 9H), 0.07 (s, 6H).

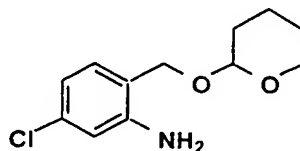
EXAMPLE 2

4-chloro-2-nitro-1-[[tetrahydro-2H-pyran-2-yl]oxy]methylbenzene

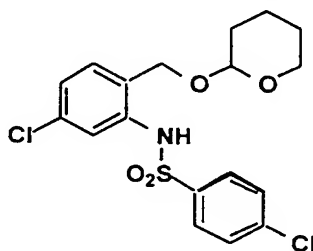


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A magnetically stirred solution of 4-chloro-2-nitrobenzyl alcohol (25.0 g, 133 mmol) and 3,4-dihydro-2H-pyran (18.2 mL, 16.8 g, 200 mmol) in anhydrous dichloromethane (250 mL) was treated at 25 °C with pyridinium p-toluenesulfonate (PPTS, 50 mg). The solution was stirred for 12 h, washed with 1 N NaOH (250 mL), brine (250 mL), dried (K₂CO₃), filtered, and concentrated in vacuo. Silica
20 gel chromatography (4:1 hexane:ethyl acetate) of the concentrate gave 22.5 g (62%) of the title compound as an oil.

EXAMPLE 3**5-chloro-2-[[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]benzenamine**

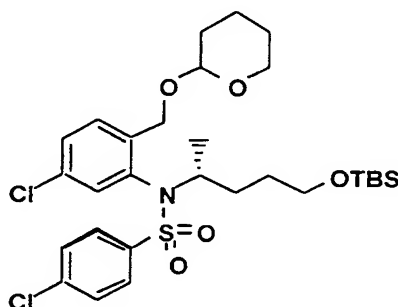
5 A Parr bottle containing 4-chloro-2-nitro-1-[[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]benzene (22.6 g, 82.8 mmol) and ethanol (150 mL) was treated with Raney nickel (50% slurry in water, 2.0 g), charged with hydrogen (60 psi) and rocked until hydrogen uptake ceased (3 h). The resultant suspension was filtered through celite, and the celite cake thoroughly washed with fresh ethanol (5 x 150 mL). The combined organic extracts were concentrated in vacuo to give an orange oil that
10 crystallized on standing. Recrystallization (ethyl acetate/hexane) gave the title compound as a white solid (19.64 g, 98%). ¹H NMR (CDCl₃) δ 7.00 (d, *J* = 8 Hz, 1H), 6.65-6.60 (m, 2H), 4.72 (A of ABq, *J* = 12 Hz, 1H), 4.79-4.77 (m, 1H), 4.45 (B of ABq, *J* = 12 Hz, 1H), 4.27 (bs, 2H), 3.94-3.85 (m, 1H), 3.58-3.50 (m, 1H), 1.88-1.65 (m, 2H), 1.58-1.46 (m, 4H).

EXAMPLE 4**4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]benzenesulfonamide**

To a magnetically stirred solution of 5-chloro-2-[[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]benzenamine (4.38 g, 18.1 mmol) in anhydrous pyridine (100 mL) at 25 °C was added 4-chlorobenzenesulfonyl chloride (3.82 g, 18.1 mmol). The solution was stirred for 24 h and
20 concentrated in vacuo. The residue was dissolved in dichloromethane (150 mL), washed with brine (3 x 150 mL) and concentrated in vacuo. Silica gel chromatography (6:1 hexane:ethyl acetate) of the concentrate afforded the title compound (5.27 g, 76%) as a crystalline solid. ¹H NMR (CDCl₃) δ 8.70 (bs, 1H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.58 (s, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.05-6.99 (m, 2H), 4.52-4.48 (m, 1H), 4.31 (A of ABq, *J* = 12 Hz, 1H), 4.24 (B of ABq, *J* = 12 Hz, 1H), 4.13-4.05 (m, 1H), 3.63-
25 3.55 (m, 1H), 1.88-1.71 (m, 2H), 1.62-1.45 (m, 4H).

EXAMPLE 5

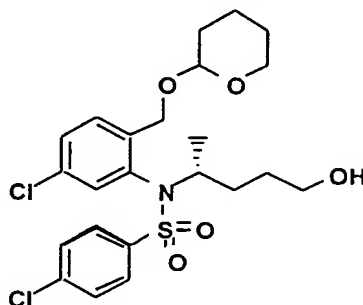
4-chloro-N-[5-chloro-2-[[*O*-(2-tetrahydropyranyl)methyl]phenyl]]-N-[[4-[dimethyl(1,1-dimethylethyl)silyl]oxy]-1(R)-methylbutyl]benzenesulfonamide



5 To a solution of 4-chloro-N-[5-chloro-2-[[*O*-(2-tetrahydropyranyl)methyl]phenyl]benzenesulfonamide (2.70 g, 6.40 mmol), triphenylphosphine (3.40 g, 12.8 mmol) and (*S*)-[[dimethyl(1,1-dimethylethyl)silyl]oxy]-2-pentanol (2.40 g, 12.8 mmol) in THF (25 mL) was added diisopropylazodicarboxylate (2.40 mL, 12.8 mmol) dropwise at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to warm to 22 °C with stirring. Stirring was continued for a period of 18
10 h and diethyl ether (100 mL) was added. The white solid was filtered, washed with ether (50 mL), and the combined ether solution was concentrated under reduced pressure. Silica gel chromatography (3:17 ethyl acetate:hexanes) of the concentrate afforded the title compound (4.00 g, 100%) as a colorless oil. MS (ESI) *m/e* 615 (M-H).

EXAMPLE 6

15 **4-chloro-N-[5-chloro-2-[[*O*-(2-tetrahydropyranyl)methyl]phenyl]]-N-(4-hydroxy-1-methylbutyl)benzenesulfonamide**

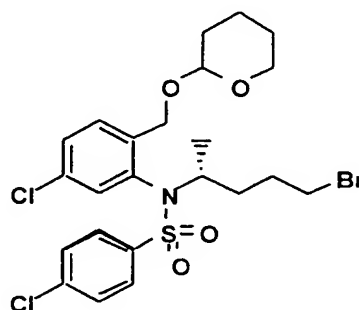


To a solution of 4-chloro-N-[5-chloro-2-[[*O*-(2-tetrahydropyranyl)methyl]phenyl]]-N-[[4-[dimethyl(1,1-dimethylethyl)silyl]oxy]-1-methylbutyl]benzene sulfonamide (3.80 g, 6.40 mmol) in
20 THF (10 mL) was added 1M tetrabutylammonium fluoride (10 mL, 10 mmol) at 0 °C. The resulting solution was allowed to stir at 0 °C for 2 h and concentrated under reduced pressure. Silica gel

chromatography (1:1 ethyl acetate:hexane) of the concentrate afforded the title compound (3.20 g, 100%) as a colorless oil. MS (ESI) m/e 500 (M-H).

EXAMPLE 7

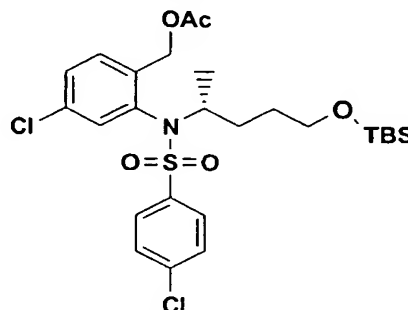
4-chloro-N-[5-chloro-2-[[*O*-(2-tetrahydropyranyl)methyl]phenyl]]-N-(4-bromo-1-methylbutyl)benzenesulfonamide



To a solution of 4-chloro-N-[5-chloro-2-[[*O*-(2-tetrahydropyranyl)methyl] phenyl]]-N-(4-hydroxy-1-methylbutyl)benzenesulfonamide (3.20 g, 6.40 mmol) and triphenylphosphine (2.10 g, 8.03 mmol) in methylene chloride (30 mL) was added carbon tetrabromide (2.60 mL, 8.03 mmol) dropwise at 0 °C. The resulting solution was allowed to stir and warm to 22 °C for 12 h. A saturated solution of ammonium chloride (25 mL) was added. The reaction was extracted with methylene chloride (2 X 100 mL). The organic phase was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (3:17 ethyl acetate:hexanes) of the concentrate afforded the title compound (2.10 g, 56%) as a colorless oil. MS (ESI) m/e 564 (M+H).

EXAMPLE 8

4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)dimethylsilyl]oxy]butyl]benzenesulfonamide

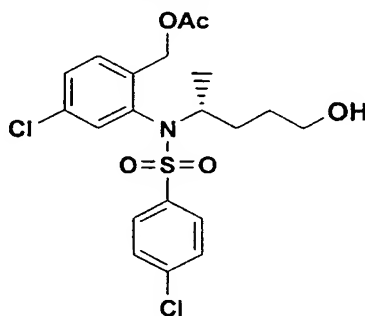


To a solution of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]benzenesulfonamide (13.7 g, 36.6 mmol), triphenylphosphine (21.1 g, 80.6 mmol) and 5S-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-pentanol (16.0 g, 73.3 mmol) in THF (130 mL) was added

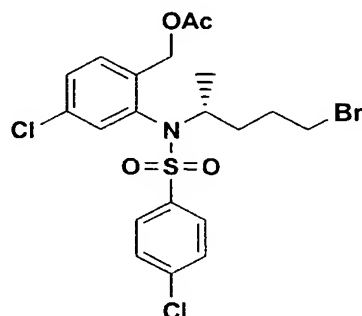
diisopropylazodicarboxylate (15.9 mL, 80.6 mmol) dropwise at 0 °C under nitrogen. The resulting mixture was allowed to warm to 22 °C with stirring. Stirring was continued for a period of 12 h followed by the addition of 150 ml of H₂O. The mixture was extracted with ether (3 X 100 mL). The combined organic extracts were washed with 1M NaHCO₃ and sat. brine. The organic phase was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:5 ethyl acetate:hexanes) of the concentrate afforded 16.6 g of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)dimethylsilyl]oxy]butyl]benzenesulfonamide as a yellow oil in 79% yield.

EXAMPLE 9

4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide



To a solution of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)dimethylsilyl]oxy]butyl]benzenesulfonamide (15.9 g, 27.8 mmol) in acetonitrile (45 mL) was added 48% aqueous HF (16 mL) dropwise at 0 °C. The resulting solution was stirred for 1h at 0 °C followed by addition of 50 mL of 1M NaHCO₃. The product was extracted with ether (2 X 50 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (ethyl acetate) of the concentrate afforded 10.4 g of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide as a colorless oil in 81% yield.

EXAMPLE 10**4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide**

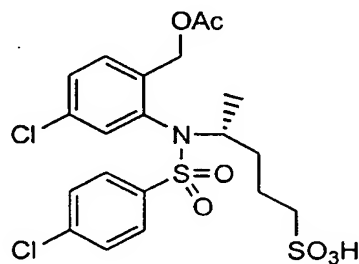
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To a solution of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide (500 mg, 1.09 mmol) in acetonitrile (2 mL) was added triphenylphosphine (571 mg, 2.18 mmol) and carbon tetrabromide (720 mg, 2.18 mmol) at 0 °C. The resulting mixture was allowed to stir at 22 °C for 12 h followed by the addition of 25 mL of sat. ammonium chloride. The product was extracted with ether (2 X 25 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:4 ethyl acetate:hexanes) of the concentrate afforded 479 mg of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide as a colorless oil in 84% yield.

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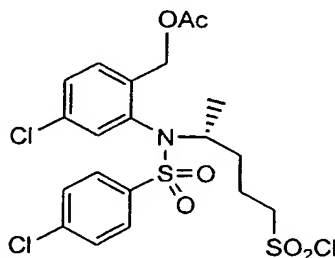
EXAMPLE 11**(4R)-4-[5-chloro-2-(acetoxymethyl)phenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonic acid**

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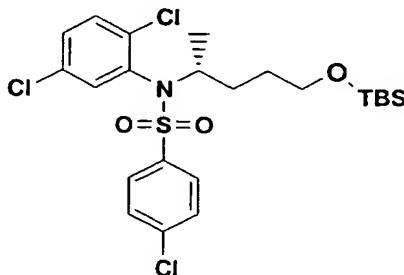


To a solution of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide (1.00g, 1.91mmol) in methanol/water (1:1, 4 mL) was added Na₂SO₃ (0.723g, 5.74mmol). The mixture was heated to reflux for 12 hours and then evaporated under reduced pressure. 2M HCl (25 mL) was added to the resulting oil. This mixture was extracted with CH₂Cl₂ (2x 50 mL), dried over Na₂SO₄, and filtered. Solvent was concentrated under reduced pressure to afford (4R)-4-[5-chloro-2-(acetoxymethyl)phenyl] [4-chlorophenyl) sulfonyl]-amine]pentylsulfonic acid (821mg) as colorless oil in 88% yield. MS (ESI), 526 (M + 1).

20

EXAMPLE 12**(4R)-4-[5-chloro-2-(hydroxymethyl)phenyl](4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride**

5 To a solution of (4R)-4-[5-chloro-2-(acetoxymethyl)phenyl] [4-chlorophenyl] sulfonyl] - amino] pentylsulfonic acid (560mg, 1.07mmol) in benzene (5 mL) was added phosphorus pentachloride (445mg, 2.14mmol) at 22 °C. The mixture was heated to reflux for 2 hours. This mixture was concentrated under reduced pressure and rediluted with CH₂Cl₂ (100mL). This solution was washed with water (100 mL), dried over Na₂SO₄ and filtered. The organic solution was concentrated to afford
10 442mg of (4R)-4-[5-chloro-2-(acetoxymethyl)phenyl](4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride as a pale yellow oil in 76% yield.

EXAMPLE 13**4-chloro-N-[5-chloro-2-chlorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)dimethylsilyl]oxy]butyl]benzenesulfonamide**

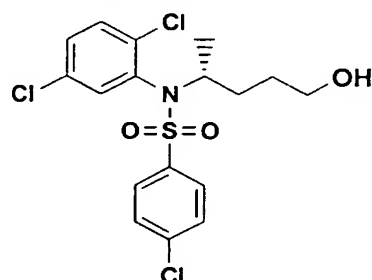
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To a solution of 4-chloro-N-[5-chloro-2-chlorophenyl]benzenesulfonamide (1.00 g, 2.97 mmol), triphenylphosphine (1.64 g, 6.24 mmol) and 5S-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-pentanol (1.30 g, 5.94 mmol) in THF (12 mL) was added diisopropylazodicarboxylate (1.23 mL, 6.24 mol) dropwise at 0 °C under nitrogen. The resulting mixture was allowed to warm to 22 °C with stirring. Stirring was continued for a period of 12 h followed by the addition of 25 mL of H₂O. The mixture was extracted with ether (3 X 25 mL). The combined organic extracts were washed with 1M NaHCO₃ and sat. brine. The organic phase was dried over Na₂SO₄, filtered, and concentrated under
20

reduced pressure. Silica gel chromatography (1:5 ethyl acetate:hexanes) of the concentrate afforded 830 mg of 4-chloro-N-[5-chloro-2-chlorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)-dimethylsilyl]oxy) butyl]benzenesulfonamide as a yellow oil in 52% yield.

EXAMPLE 14

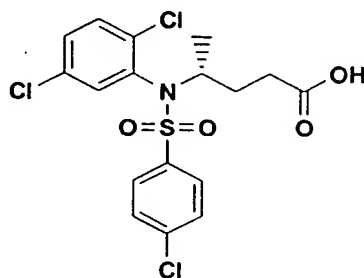
5 4-chloro-N-[5-chloro-2-chlorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide



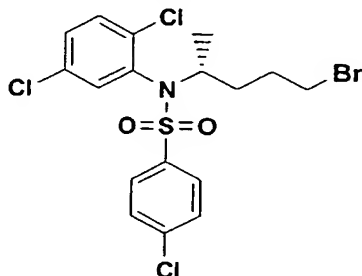
To a solution of 4-chloro-N-[5-chloro-2-chlorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)dimethylsilyl]oxy)butyl]benzenesulfonamide (650 mg, 1.21 mmol) in acetonitrile (4 mL) was added 48% aqueous HF (2 mL) dropwise at 0 °C. The resulting solution was stirred for 1h at 0 °C followed by addition of 10 ml of 1M NaHCO₃. The product was extracted with ether (2 X 25 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (ethyl acetate) of the concentrate afforded 430 mg of 4-chloro-N-[5-chloro-2-chlorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide as a yellow oil in 84% yield.

EXAMPLE 15

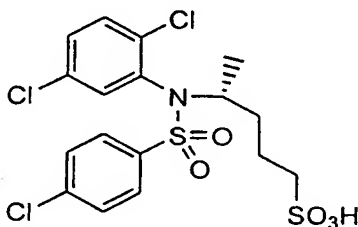
15 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(carboxy)-1(R) methylpropyl)benzenesulfonamide



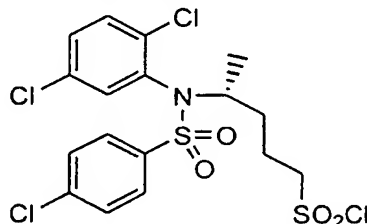
4-chloro-N-[5-chloro-2-chlorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide (1.57 g, 0.0037 moles) was dissolved in acetonitrile (25 mL) and water (2 mL). RuCl₃ (50 mg), and NaIO₄ (1.19 g, 0.0056 moles, 1.5 eq) were added and the mixture was stirred at room temperature for 18 hours. The mixture was filtered, concentrated, dissolved in CH₂Cl₂, washed with 1N HCl, dried over Na₂SO₄ and evaporated. Chromatography over silica gel using 50-100% ethyl acetate/ Hexane gave pure product (1.00 g, 62%) as a beige solid.

EXAMPLE 16**4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl] benzenesulfonamide**

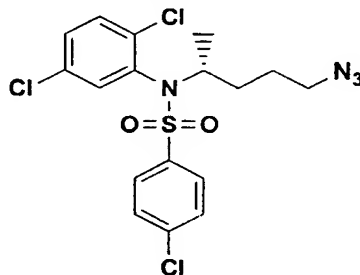
To a solution of 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzene-
sulfonamide (3.90 g, 9.20 mmol) in CH₂Cl₂ (20 mL) was added triphenylphosphine (4.87 g, 18.4 mmol)
and carbon tetrabromide (6.09 g, 18.4 mmol) at 0 °C. The resulting mixture was allowed to stir at 22
°C overnight. To the reaction was added sat. ammonium chloride (200 mL). The product was
extracted with CH₂Cl₂ (2 x 200 mL), dried over Na₂SO₄, filtered, and concentrated under reduced
pressure. Silica gel chromatography (1:4 ethyl acetate:hexanes) of the concentrate afforded 3.13g of 4-
chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide as a colorless oil in
70% yield. MS (ESI) 486 (M+H).

EXAMPLE 17**(4R)-4-[2,5-dichlorophenyl] [4-chlorophenyl] sulfonyl]-amine]pentylsulfonic acid**

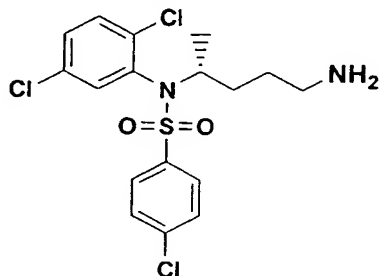
To a solution of 4-chloro-N-[5-chloro-2-chlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzene-
sulfonamide (2.85 g, 5.88 mmol) in methanol/water (1:1, 12 mL) was added Na₂SO₃ (7.40 g, 58.8
mmol). The mixture was heated to reflux for 12 hours and then evaporated under reduced pressure.
2M HCl was added to the resulting oil. This mixture was extracted with CH₂Cl₂ (2 X 50mL), dried over
Na₂SO₄, and filtered. Solvent was concentrated under reduced pressure to afford (4R)-4-[2,5
dichlorophenyl] [4-chlorophenyl] sulfonyl]-amine]pentylsulfonic acid (2.34 g) as colorless oil in 82%
yield. MS (ESI) 486 (M + 1).

EXAMPLE 18**(4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride**

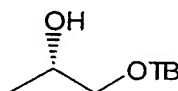
To a solution of (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino] pentylsulfonic acid (2.34 g, 4.80 mmol) in benzene (10 mL) was added phosphorus pentachloride (1.48 g, 7.21 mmol) at 22 °C. The mixture was heated to reflux for 2 hours. This mixture was concentrated under reduced pressure and rediluted with CH₂Cl₂ (120 mL). This solution was washed with water (100 mL), dried over Na₂SO₄ and filtered. The organic solution was concentrated to afford 2.21g of (4R)-4-[2, 5-dichlorophenyl][4- chlorophenyl) sulfonyl]-amino] pentylsulfonyl chloride as pale yellow oil in 91% yield. LC/MS 504.

EXAMPLE 19**4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-azidobutyl] benzenesulfonamide**

To a solution of 4-chloro-N-[2,5-dichlorophenyl]-N-[R]-1-methyl-4-bromobutyl]benzenesulfonamide (1.06 g, 2.50 mmol) in DMF (2.5 mL) was added diphenylphosphoryl azide (1.08 mL, 5.00 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.935 mL, 6.25 mmol) at 0 °C. The resulting mixture was allowed to stir at 100 °C overnight. To the reaction was added sat. ammonium chloride (200 mL). The product was extracted with CH₂Cl₂ (2 X 100 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:4 ethyl acetate:hexanes) of the concentrate afforded 977 mg of 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-azidobutyl]-benzenesulfonamide as a colorless oil in 87% yield. MS (ESI) 447 (M+H).

EXAMPLE 20**4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-aminobutyl] benzenesulfonamide**

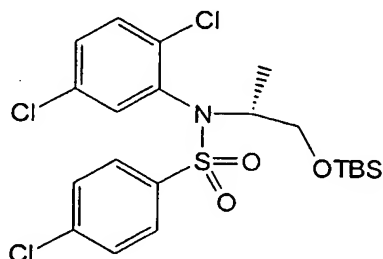
To a solution of 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-aminobutyl]benzene-
5 sulfonamide (1.20 g, 2.68 mmol) in THF (5 mL) was added a THF solution of lithium aluminum
hydride (1.0 M, 2.68 mL) at -20 °C. The resulting mixture was allowed to stir at -20 °C overnight. To
the reaction was added 0.5M NaOH (6 mL). This mixture was filtered through celite, dried over
Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:9
10 methanol/CHCl₃) of the concentrate afforded 972 mg of 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-
methyl-4-aminobutyl]benzenesulfonamide as a colorless oil in 86% yield. MS (ESI) 421 (M+H).

EXAMPLE 21**(S)-[3-[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propanol**

To a solution of (S)-1,2-propanediol (20.0 g, 0.263 mol), triethylamine (31.9 g, 0.315 mol), 4-
15 dimethylaminopyridine (1.28 g, 10.5 mmol) in CH₂Cl₂ (200 mL) was added *tert*-butyldimethylsiloxy
chloride (47.3 g, 0.315 mol) at 22 °C. The mixture was allowed to stir for 18 h. The mixture was
diluted with CH₂Cl₂, washed with water and sat. aqueous NH₄Cl. The organic solution was dried over
Na₂SO₄, filtered and concentrated under reduced pressure. Silica gel chromatography (5% ethyl
acetate/ hexanes) of the concentrate gave 45.0 g of the title compound as a clear oil in 90% yield.

EXAMPLE 22

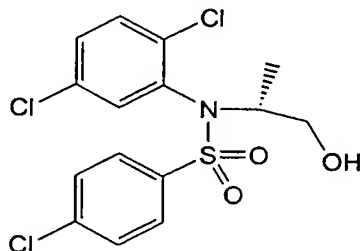
4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-4-[(1,1-dimethylethyl) dimethylsilyl]oxy]-ethyl] benzenesulfonamide



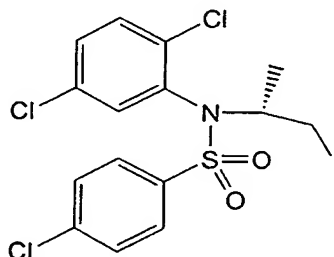
- 5 To a solution of 4-chloro-N-[2,5-dichlorophenyl]benzenesulfonamide (5.74 g, 17.1 mmol), triphenylphosphine (6.70 g, 25.7 mmol), (S)-[3-[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propanol (4.90 g, 25.7 mmol) in THF (50 mL) was added diisopropylazodicarboxylate (5.19 g, 25.7 mmol) dropwise at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to warm to 22 °C. Stirring was continued for a period of 18 h followed by the addition of water. The mixture was
10 extracted with diethyl ether. The combined organic extracts were washed with NaHCO₃, sat. brine and dried over Na₂SO₄. Silica gel chromatography (1:10 ethyl acetate:hexanes) of the concentrate produced the title compound in 90% yield.

EXAMPLE 23

- 15 **4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-(2-hydroxyethyl)]benzenesulfonamide**

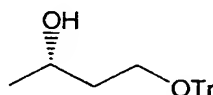


- To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-[[4-(1,1-dimethylethyl)-dimethylsilyl]oxy]ethyl]benzenesulfonamide (07.80 g, 15.3 mmol) in CH₃CN was added HF (5.5 mL) at 0 °C. The resulting mixture was allowed to stir at 0 °C for 2h and concentrated under reduced
20 pressure. Silica gel chromatography (1:1 ethyl acetate:hexanes) of the concentrate afforded the title compound (5.70 g, 95%) as a colorless oil.

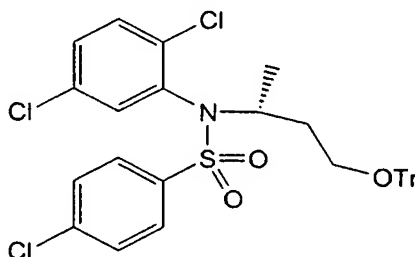
EXAMPLE 24**4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl(2-iodoethyl)]benzene sulfonamide**

5 To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl(2-hydroxyethyl) benzene-sulfonamide (0.660 g, 1.67 mmol), triphenylphosphine (0.530 g, 2.00 mmol) and imidazole (0.136 g, 2.00 mmol) in diethyl ether/CH₃CN(2:1, 3.0 mL) was added iodine (0.430 g, 1.67 mol) at 0 °C under nitrogen and stirred for 12 hr. This mixture was concentrated under reduced pressure and diluted with CH₂Cl₂. This solution was washed with water (50 ml), dried over Na₂SO₄ and filtered. The organic solution was concentrated to afford the title compound as a light yellow oil in 96% yield.

10

EXAMPLE 25**(S)-4-triphenylmethyloxy-2-butanol**

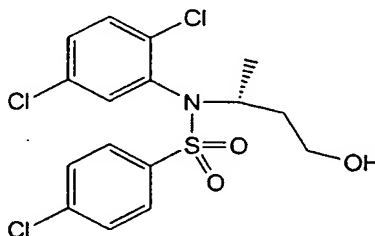
15 To a solution of (S)-(+)-1,3-butanediol (10.0 g, 0.110 mol), was added triphenylmethylchloride (33.0 g, 0.330 mol), 4-dimethylaminopyridine (1.40 g, 11.5 mmol) in CH₂Cl₂/pyridine (1:1, 500 mL). Stirring was continued over 48h. The solvent was removed, the mixture was diluted with ether, washed with brine and dried over Na₂SO₄. The organic solution was filtered and concentrated. Silica gel chromatography with (5% ethyl acetate/hexanes) produced a clear oil (24g) in 70% yield.

EXAMPLE 26**4-chloro-N-(2,5-dichlorophenyl)-N-[1(R)-methyl-(3-triphenylmethoxy)-propyl]benzenesulfonamide**

5

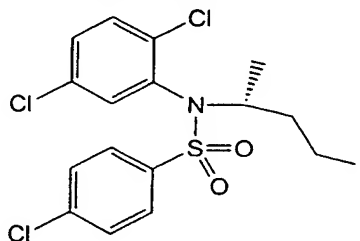
To a solution of 4-chloro-N-(2,5-dichlorophenyl)benzenesulfonamide (7.00 g, 20.8 mmol), triphenylphosphine (7.00 g, 27.0 mmol), (S)-4-triphenylmethoxy-2-butanol (8.60 g, 27.0 mmol) in THF (30 mL) was added diisopropylazodicarboxylate (5.48 g, 27.0 mmol) dropwise at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to warm to 22 °C with stirring. After 18 h the mixture was washed with water, brine, dried over Na₂SO₄ and filtered. Silica gel chromatography (1:10 ethyl acetate/ hexanes) of the concentrate produced the title compound in 90% yield.

10

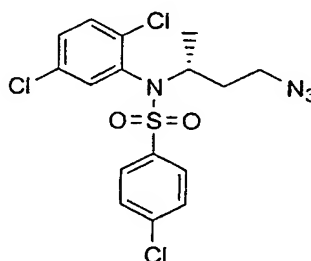
EXAMPLE 27**4-chloro-N-(2,5dichlorophenyl)-N-[1(R)-methyl-(3-hydroxy)-propyl]benzenesulfonamide**

15

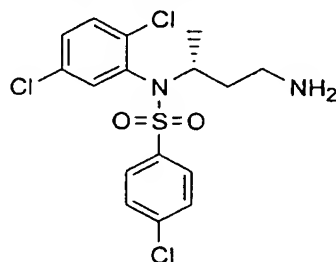
To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[1(R)-methyl-(3-triphenylmethoxy)-propyl]benzenesulfonamide (2.00 g, 3.00 mmol) in CH₃CN (20 mL) was added Amberlyst 15 ion-exchange resin (6.0 g). The resulting mixture was allowed to stir at 22 °C for 12 h and filtered. Silica gel chromatography (1:1 ethyl acetate: hexanes) of the concentrate afforded the title compound as a colorless oil in quantitative yield.

EXAMPLE 28**4-chloro-N-(2,5-dichlorophenyl)-N-[1(R)-methyl-(3-iodo)-propyl]benzene sulfonamide**

To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[1(R)-methyl-(3-hydroxy)-propyl]benzene-sulfonamide (1.40 g, 3.40 mmol), triphenylphosphine (0.900 g, 3.40 mmol) and imidazole (0.230 g, 3.40 mmol) in diethyl ether/CH₃CN (2:1, 7.0 mL) was added iodine (0.860 g, 3.40 mmol) at 0 °C under nitrogen and stirred for 12 h. The solvent was removed, the residue was taken into CH₂Cl₂, washed with water, dried over Na₂SO₄ and filtered. The organic solution was concentrated to afford the title compound as a light yellow oil in 96% yield.

EXAMPLE 29**4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-3-azidopropyl]benzenesulfonamide**

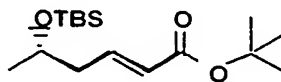
To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide (1.188 g, 2.295 mmol) in THF/H₂O (20/4, 24 mL) was added sodium azide (1.49 g, 22.9 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for 4 days. The mixture was extracted with ether (3 X 60 mL). The combined organic extracts were washed with sat. NaHCO₃, dried over MgSO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) of the concentrate afforded 0.941 g of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-3-azidopropyl]benzenesulfonamide as a colorless oil in 94% yield.

EXAMPLE 30**4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide**

To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-3-azidopropyl]benzenesulfonamide (0.941 g, 2.16 mmol) in THF (21 mL) was added lithium aluminum hydride (4.33 mL, 1 M in THF) at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 0 °C for 1 h and subsequently treated by successive dropwise addition of 0.165 mL of water, 0.165 mL of 15% sodium hydroxide solution, and 0.493 mL of water. The mixture was filtered and concentrated under reduced pressure. Silica gel chromatography (3:10 ethyl acetate:hexanes) of the concentrate afforded 0.748 g of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide as a light brown oil in 85% yield.

EXAMPLE 31**(3S)-(1,1-dimethylethyl)dimethylsiloxy butanal**

A solution of methyl (S)-3-tert-butyl dimethylsiloxy butyrate (35.0 g 151 mmol) in hexane (400 mL) was cooled to -78 °C. DIBAL-H (195 mL, 195 mmol, 1M in hexanes) was added dropwise. Stirring was continued for 1 h after which time water (75 mL) was cautiously added dropwise, after addition was complete stirring was continued at 22 °C for 18h. The reaction was diluted with diethyl ether and then decanted several times. The solvents were removed to afford (3S)-(1,1-dimethylethyl)dimethylsiloxy butanal as a clear oil in quantitative yield. ¹H NMR (CDCl₃) δ 9.85 (s br, 1H), 4.40-4.51 (m, 1H), 2.42-2.65 (m, 2H), 1.29 (d, 3H, J=6.0Hz), 0.96 (s, 9H), 0.14 (d, 6H, J=3Hz).

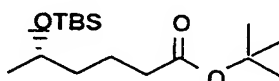
EXAMPLE 32**(trans)1,1-dimethylethyl-(5S)-(1,1-dimethylethyl)dimethylsiloxy-hex-2-enoate,**

To a solution of (3S)-(1,1-dimethylethyl)dimethylsiloxy butanal (24.0 g 121 mmol), in dichloromethane (400 mL) at 0 °C was added tert-butoxy carbonylmethylene triphenylphosphorane

(50.0 g, 133 mmol). Stirring was continued for 2h after which time the reaction was concentrated and the resulting oil was purified by silica gel chromatography (5% ethyl acetate / Hexane) to afford (trans)1,1-dimethylethyl-(5S)-(1,1-dimethylethyl)dimethylsiloxy-hex-2-enoate as a clear oil in 93% yield. ¹H NMR (CDCl₃) δ6.79-6.90 (m, 1H) 5.75 (d, ¹H, J=15.6Hz), 3.85-3.87 (m, 1H), 2.26-2.32 (m, 2H), 1.47 (s, 9H), 1.15 (d, 3H, J=6.0Hz), 0.90 (s, 9H), 0.06 (s, 6H).

EXAMPLE 33

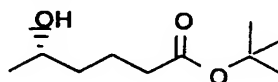
1,1-dimethylethyl-butyl-(5S)-(1,1-dimethylethyl)dimethylsiloxy-hexanoate,



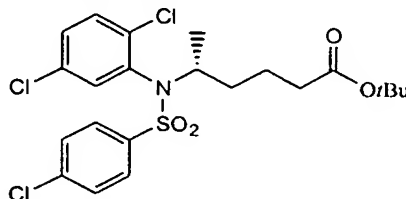
A suspension of (trans)tert-butyl-(5S)-tert-butyldimethylsiloxy-hex-2-enoate (33.5 g, 111 mmol), 10% Pd/C (5 g), in ethanol (250 mL), was hydrogenated at 45 psi for 1h. The catalyst was filtered off and the filtrate was concentrated to afford 1,1-dimethylethyl-butyl-(5S)-(1,1-dimethylethyl)dimethylsiloxy-hexanoate as a white wax in quantitative yield. ¹H NMR (CDCl₃) δ3.72-3.84 (m, 1H), 2.20 (t, 2H, J=7.0Hz), 1.60-1.74 (m, 2H), 1.35-1.70 (m, 4H), 1.44 (s, 9H), 1.35 (d, 3H, J=6.0Hz), 0.88 (s, 9H), 0.10 (s, 6H).

EXAMPLE 34

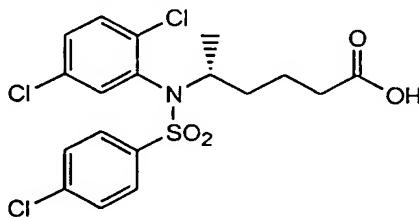
1,1-dimethylethyl (5S)-5-hydroxyhexanoate



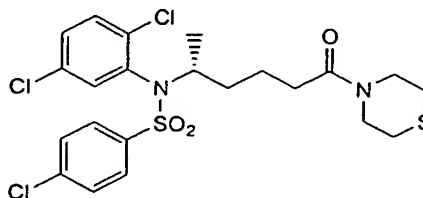
A solution of 1,1-dimethylethyl-(5S)-(1,1-dimethylethyl)dimethylsiloxy-hexanoate (19.0 g, 63.0 mmol) in THF (250 mL) was treated with tetrabutylammonium fluoride (94 mL, 94 mmol, 1M in THF) at 0 °C. The reaction mixture was allowed to warm to 22 °C, and stirring was continued for 18h. The reaction mixture was diluted with diethyl ether, washed with water, and dried over MgSO₄. Silica gel chromatography (20% ethyl acetate/hexane) of the concentrate produced 1,1-dimethylethyl (5S)-5-hydroxyhexanoate in 89% yield. ¹H NMR (CDCl₃) δ3.74-3.86 (m, 1H), 2.32 (t, 2H, J=6.6Hz), 1.60-1.74 (m, 2H), 1.57 (s, 1H, OH), 1.44-1.48 (m, 2H), 1.45 (s, 9H), 1.20 (d, 3H, J=6.0Hz).

EXAMPLE 35**1,1-dimethylethyl(5R)-5-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]hexanoate**

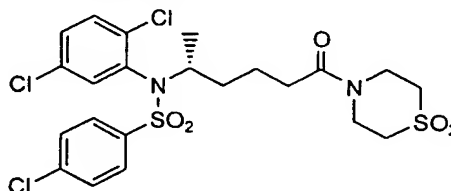
To a solution 2,5-dichloro-N[[4-chlorophenyl]amino]phenyl)sulfonamide (2.42 g, 7.20 mmol), triphenyl phosphine (3.70 g, 14.4 mmol) and 1,1-dimethylethyl(5S)-5-hydroxyhexanoate (2.70 g, 14.4 mmol) in THF (100 mL) was added diisopropylazodicarboxylate (2.51 g, 14.4 mmol) dropwise at 0 °C under nitrogen. The reaction mixture was allowed to warm to 22 °C with stirring for a period of 18h. The reaction mixture was diluted with ethyl acetate then washed with water, brine and dried over MgSO₄. Silica gel chromatography (20% ethyl acetate/hexane) of the concentrate produced 1,1-dimethylethyl(5R)-5-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]hexanoate in 60% yield.

EXAMPLE 36**(5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]-amino]hexanoic acid**

1,1-dimethylethyl(5R)-5-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]hexanoate (700 g, 1.40 mmol) was treated with a 50% solution of trifluoroacetic acid in dichloromethane (20 mL). After 3h the reaction was diluted with dichloromethane then washed with water, brine and dried over MgSO₄. Concentration under reduced pressure afforded (5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]-amino]hexanoic acid in quantitative yield. MS (ESI), (M-H⁻) 450. IR- 2975,1706,1466,1348.

EXAMPLE 37**4-chloro-N(2,5-dichlorophenyl)-N-[5-(1R)-methyl-5-oxo-(4-thiomorpholinyl)pentyl]benzenesulfonamide**

5 To a solution of (5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]-amino]hexanoic acid (2.00 g, 4.40 mmol), N,N-diisopropylethylamine (1.62 mL, 8.80 mmol) and 1-hydroxybenzotriazole (645 mg, 4.80 mmol), in dichloromethane (100 mL) was added 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (920 mg, 4.80 mmol). After 18 h the solvent is removed and the residue is taken into ethyl acetate and successively washed with aqueous HCl, water, brine and then
10 concentrated to afford the title compound as a white solid (1.43g) in 61% yield. MS (ESI), (MH⁺) 537.2. IR- 2910,1643,1581,1466,1348.

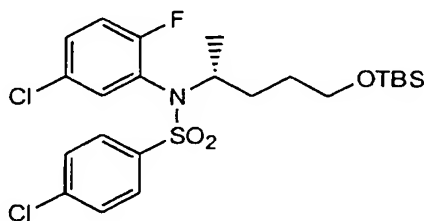
EXAMPLE 38**4-chloro-N(2,5-dichlorophenyl)-N-[5-(1R)-methyl-5-oxo-(1,1-dioxido-4-thiomorpholinyl)pentyl]benzenesulfonamide**

15

A solution of 4-chloro-N(2,5-dichlorophenyl)-N-[5-(1R)-methyl-5-oxo-(4-thiomorpholinyl)-pentyl]benzenesulfonamide (1.10 g, 2.10 mmol) in dichloromethane (100 mL) was treated with 3-chloroperoxybenzoic acid (1.10 g, 5.10 mmol) at 0 °C. After stirring for 1 h the ice bath was removed and stirring was continued for 18 h. The reaction mixture was diluted with dichloromethane, and
20 washed with 1N NaOH, H₂O, brine, and dried over MgSO₄. Concentration produced the title compound (1.01 g) in 91% yield. MS (ESI), (M+H)⁺ 569.2. IR-3441,2935,1653,1467,1428,1318.

EXAMPLE 39

4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)dimethylsilyl]oxy]butyl]benzenesulfonamide

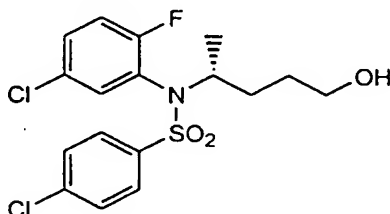


5 To a solution of 4-chloro-N-[5-chloro-2-fluorophenyl]benzenesulfonamide (500 mg, 1.56 mmol), triphenylphosphine (859 mg, 3.28 mmol) and 5S-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-pentanol (682 mg, 3.12 mmol) in THF (7 mL) was added diisopropylazodicarboxylate (0.645 mL, 3.28 mol) dropwise at 0 °C under nitrogen. The resulting mixture was allowed to warm to 22 °C with stirring. Stirring was continued for a period of 12 h followed by the addition of 15 mL of H₂O. The
10 mixture was extracted with ether (3 X 15 mL). The combined organic extracts were washed with NaHCO₃ and sat. brine. The organic phase was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:5 ethyl acetate:hexanes) of the concentrate afforded 495 mg of 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)-dimethylsilyl]oxy]butyl]benzenesulfonamide as a yellow oil in 61% yield.

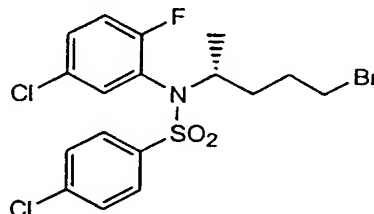
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EXAMPLE 40

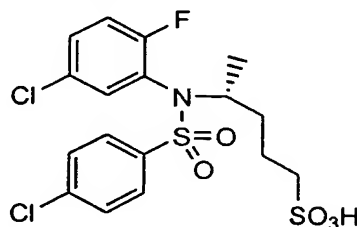
4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide



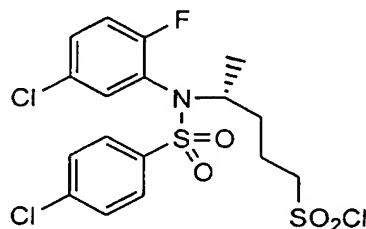
To a solution of 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)-dimethylsilyl]oxy]butyl]benzenesulfonamide (495 mg, 0.951 mmol) in acetonitrile (4 mL) was added
20 48% aqueous HF (2 mL) dropwise at 0°C. The resulting solution was stirred for 1h at 0 °C followed by addition of 10 mL of 1M NaHCO₃. The product was extracted with ether (2 X 25 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (ethyl acetate) of the concentrate afforded 336 mg of 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide as a yellow oil in 87% yield.

EXAMPLE 41**4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide**

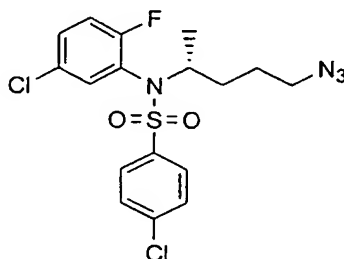
To a solution of 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]-
5 benzenesulfonamide (336 mg, 0.827 mmol) in acetonitrile (4 mL) was added triphenylphosphine (433
mg, 1.65 mmol) and carbon tetrabromide (548 mg, 1.65 mmol) at 0 °C. The resulting mixture was
allowed to stir at 22 °C for 12 h followed by the addition of 25 mL of sat. ammonium chloride. The
product was extracted with ether (2 X 25 mL), dried over Na₂SO₄, filtered, and concentrated under
10 349 mg of 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide
as a yellow oil in 88% yield.

EXAMPLE 42**(4R)-4-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonic acid**

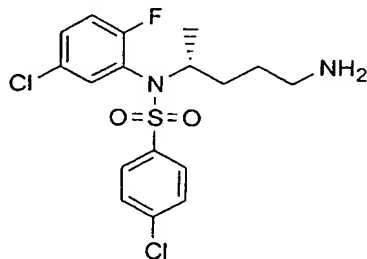
15 (4R)-4-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonic acid was
prepared analogous to (4R)-4-[2,5 dichlorophenyl] [4-chlorophenyl] sulfonyl]-amine]pentylsulfonic
acid by reacting 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-
bromobutyl]benzenesulfonamide with Na₂SO₃. Yield=86%; MS (ESI) 470 (M +1).

EXAMPLE 43**(4R)-4-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonyl chloride**

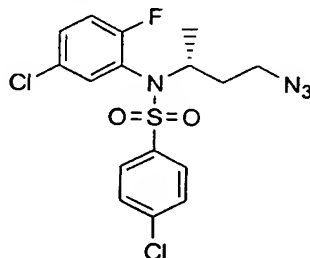
- 5 (4R)-4-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonyl chloride was prepared analogous to (4R)-4-[N-[2,5-dichlororophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonyl chloride by reacting (4R)-4-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonic acid with phosphorus pentachloride: Yield=81%; MS (ESI) 489 (M +1).

EXAMPLE 4410 **4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-4-azidobutyl]benzenesulfonamide**

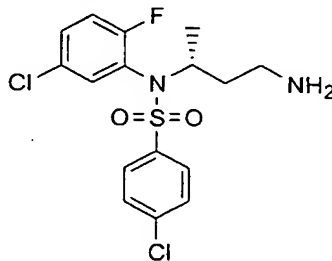
- 15 To a solution of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide (0.343 g, 0.730 mmol) in THF/H₂O (8/2 mL) was added sodium azide (0.237 g, 7.30 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for 10 days. The mixture was extracted with ether (3 X 20 mL). The combined organic extracts were washed with sat. NaHCO₃, dried over MgSO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) of the concentrate afforded 0.227 g of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-4-azidobutyl]benzenesulfonamide as a colorless oil in 72% yield.

EXAMPLE 45**4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-4-aminobutyl]benzenesulfonamide**

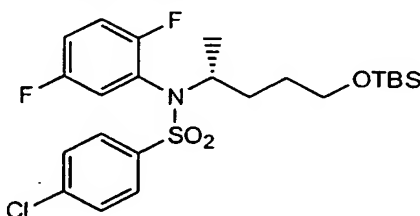
To a solution of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-4-azidobutyl]-
5 benzenesulfonamide (0.325 g, 7.77 mmol) in THF (7 mL) was added lithium aluminum hydride (1.55 mL, 1 M in THF) at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 0 °C for 1 h and subsequently treated by successive dropwise addition of 0.060 mL of water, 0.060 ml of 15% sodium hydroxide solution, and 0.180 mL of water. The mixture was filtered and concentrated under reduced pressure. Silica gel chromatography (3:10 ethyl acetate:hexanes) of the concentrate
10 afforded 0.207 g of the title compound as a light brown oil in 91% yield.

EXAMPLE 46**4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-3-azidopropyl]benzenesulfonamide**

To a solution of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-3-bromopropyl]-
15 benzenesulfonamide (1.64 g, 3.27 mmol) in THF/H₂O (20/4, 24 mL) was added sodium azide (2.13 g, 32.7 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for 4 days. The mixture was extracted with ether (3 X 60 mL). The combined organic extracts were washed with sat. NaHCO₃, dried over MgSO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) of the concentrate afforded 1.38 g of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-
20 [(R)-1-methyl-3-azidopropyl]benzenesulfonamide as a colorless oil in 95% yield.

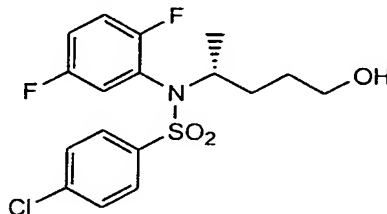
EXAMPLE 47**4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide**

To a solution of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-3-aminopropyl]-
 5 benzenesulfonamide (1.34 g, 3.27 mmol) in THF (32 mL) was added lithium aluminum hydride (6.53 mL, 1 M in THF) at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 0 °C for 1 h and subsequently treated by successive dropwise addition of 0.248 mL of water, 0.248 mL of 15% sodium hydroxide solution, and 0.744 mL of water. The mixture was filtered and concentrated under reduced pressure. Silica gel chromatography (3:10 ethyl acetate:hexanes) of the concentrate
 10 afforded 1.12 g of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide as a light brown oil in 85% yield.

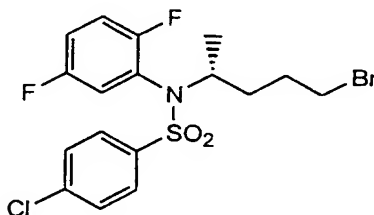
EXAMPLE 48**4-chloro-N-[5-fluoro-2-fluorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)dimethylsilyl]oxy]butyl]benzenesulfonamide**

15

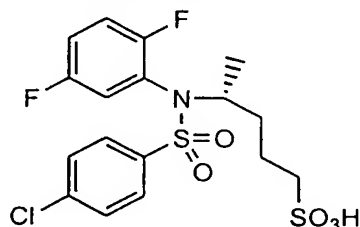
To a solution of 4-chloro-N-[5-fluoro-2-fluorophenyl]benzenesulfonamide (500 mg, 1.65 mmol), triphenylphosphine (909 mg, 3.47 mmol) and 5S-[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-pentanol (719 mg, 3.30 mmol) in THF (7 mL) was added diisopropylazodicarboxylate (0.682 mL, 3.47 mol) dropwise at 0 °C under nitrogen. The resulting mixture was allowed to warm to 22 °C with
 20 stirring. Stirring was continued for a period of 12 h followed by the addition of 15 mL of H₂O. The mixture was extracted with ether (3 X 15 mL). The combined organic extracts were washed with NaHCO₃ and sat. brine. The organic phase was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:5 ethyl acetate:hexanes) of the concentrate afforded
 25 466 mg of 4-chloro-N-[5-fluoro-2-fluorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)-dimethylsilyl]oxy]butyl]benzene-sulfonamide as a yellow oil in 56% yield.

EXAMPLE 49**4-chloro-N-[5-fluoro-2-fluorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]benzenesulfonamide**

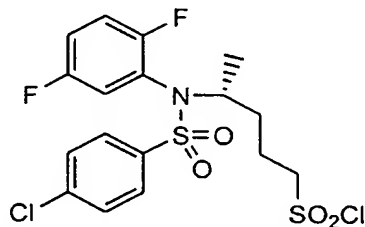
To a solution of 4-chloro-N-[5-fluoro-2-fluorophenyl]-N-[(R)-1-methyl-4-[(1,1-dimethylethyl)-
5 dimethylsilyl]oxy)butyl]benzenesulfonamide (466 mg, 0.924 mmol) in acetonitrile (4 mL) was added
48% aqueous HF (2 mL) dropwise at 0 °C. The resulting solution was stirred for 1h at 0°C followed by
addition of 10 ml of 1M NaHCO₃. The product was extracted with ether (2 X 25 mL), dried over
Na₂SO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (ethyl acetate) of
the concentrate afforded 317 mg of 4-chloro-N-[5-fluoro-2-fluorophenyl]-N-[(R)-1-methyl-4-
10 hydroxybutyl]benzenesulfonamide as a yellow oil in 88% yield.

EXAMPLE 50**4-chloro-N-[5-fluoro-2-fluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide**

To a solution of 4-chloro-N-[5-fluoro-2-fluorophenyl]-N-[(R)-1-methyl-4-hydroxybutyl]-
15 benzenesulfonamide (317 mg, 0.813 mmol) in acetonitrile (4 mL) was added triphenylphosphine (425
mg, 1.62 mmol) and carbon tetrabromide (537 mg, 1.62 mmol) at 0 °C. The resulting mixture was
allowed to stir at 22 °C for 12 h followed by the addition of 25 mL of sat. ammonium chloride. The
product was extracted with ether (2 X 25 mL), dried over Na₂SO₄, filtered, and concentrated under
reduced pressure. Silica gel chromatography (1:4 ethyl acetate:hexanes) of the concentrate afforded
20 323 mg of 4-chloro-N-[5-fluoro-2-fluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide as
a yellow oil in 86% yield.

EXAMPLE 51**(4R)-4-[N-[2,5-difluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonic acid**

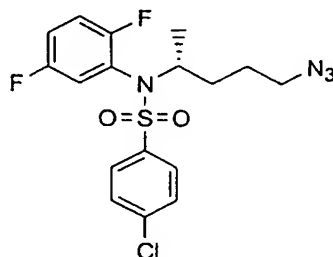
5 (4R)-4-[N-[2,5-difluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonic acid was prepared analogous to (4R)-4-[2,5-dichlorophenyl][(4-chlorophenyl)sulfonyl]-amine]pentylsulfonic acid by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with Na_2SO_3 . Yield=84%; MS (ESI) 453 (M +1).

EXAMPLE 52**(4R)-4-[N-[2,5-difluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonyl chloride**

10

(4R)-4-[N-[2,5-difluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonyl chloride was prepared analogous to (4R)-4-[2,5-dichlorophenyl][(4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride by reacting (4R)-4-[N-[2,5-difluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentylsulfonic acid with phosphorus pentachloride. Yield=88%; MS (ESI) 434 (M +1).

15

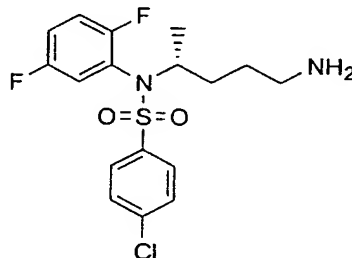
EXAMPLE 53**4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-azidobutyl]benzenesulfonamide**

To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-bromobutyl]-benzenesulfonamide (0.505 g, 1.12 mmol) in THF/H₂O (8/2, 10 mL) was added sodium azide (0.363 g,

5.58 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for 10 days. The mixture was extracted with ether (3 X 20 mL). The combined organic extracts were washed with sat. NaHCO₃, dried over MgSO₄, filtered, and concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) of the concentrate afforded 0.455 g of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-azidobutyl]benzenesulfonamide as a colorless oil in 98% yield.

EXAMPLE 54

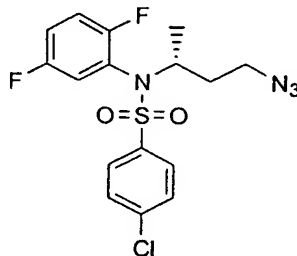
4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-aminobutyl]benzenesulfonamide



To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-azidobutyl]benzenesulfonamide (0.394 g, 0.949 mmol) in THF (10 mL) was added lithium aluminum hydride (1.90 mL, 1 M in THF) at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 0 °C for 1 h and subsequently treated by successive dropwise addition of 0.072 mL of water, 0.072 mL of 15% sodium hydroxide solution, and 0.216 mL of water. The mixture was filtered and concentrated under reduced pressure. Silica gel chromatography (3:10 ethyl acetate:hexanes) of the concentrate afforded 0.329 g of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-aminobutyl]benzenesulfonamide as a light brown oil in 89% yield.

EXAMPLE 55

4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-3-azidopropyl]benzenesulfonamide

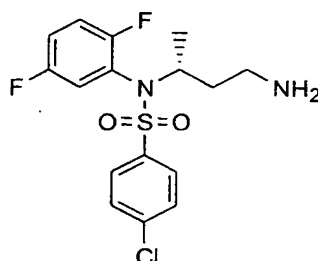


To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide (1.74 g, 3.58 mmol) in THF/H₂O (20/4, 24 mL) was added sodium azide (2.33 g, 35.8 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for 4 days. The mixture was extracted with ether (3 X 60 mL). The combined organic extracts were washed with sat. NaHCO₃,

dried over MgSO_4 , filtered, and concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) of the concentrate afforded 1.53 g of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-3-azidopropyl]benzenesulfonamide as a colorless oil in 95% yield.

EXAMPLE 56

5 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide

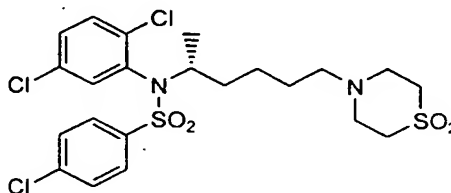


To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-3-azidopropyl]benzenesulfonamide (0.144 g, 3.59 mmol) in THF (35 mL) was added lithium aluminum hydride (7.16 mL, 1 M in THF) at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 0 °C for 1 h and subsequently treated by successive dropwise addition of 0.272 mL of water, 0.272 mL of 15% sodium hydroxide solution, and 0.816 mL of water. The mixture was concentrated under reduced pressure. Silica gel chromatography (3:10 ethyl acetate:hexanes) of the concentrate afforded 1.12 g of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide as a light brown oil in 97% yield.

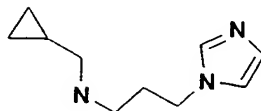
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EXAMPLE 57

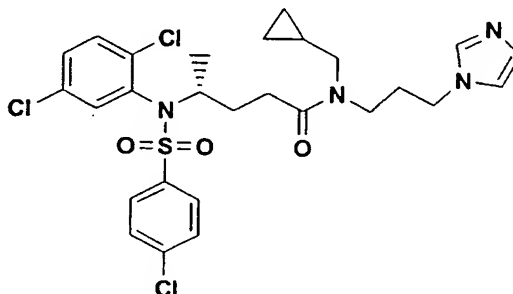
4-chloro-N(2,5-dichlorophenyl)-N-(5-(1,1-dioxido-4-thiomorpholinyl)-1(R)-methylpentyl)benzenesulfonamide



A solution of 4-chloro-N(2,5-dichlorophenyl)-N-[5-(1R)-methyl-5-oxo-(1,1-dioxido-4-thiomorpholinyl)pentyl]benzenesulfonamide (700 mg, 1.20 mmol) in THF (45 mL) was treated with a solution of borane-methyl sulfide complex (2M in THF, 1.8 mL, 3.6 mmol) dropwise at room temperature. After stirring for 18 h the reaction was cooled to 0 °C and quenched with methanol (50 mL), followed by treatment with HCl gas. The solvents were removed and the material was then purified by flash chromatography (silica gel, 15% ethyl acetate/hexane) to afford the title compound (300 mg) as a white solid in 50% yield. MS (ESI), $(\text{M}+\text{H})^+$ 553.0. IR-3430,2933,1467,1348,1326.

EXAMPLE 58**N-cyclopropylmethyl-3-(1H)-imidazolylpropylamine**

1-(3-aminopropyl)imidazole (Aldrich, 10.0 g, 0.0799 moles) was dissolved in CH₂Cl₂ (100 mL) along with pyridine (7.57 g, 0.0959 moles, 1.2 eq.). Cyclopropanecarbonyl chloride (Aldrich, 8.76 g, 0.0839 moles, 1.05 eq.) was added dropwise and the mixture was stirred for 18 hours. The solvent was removed and the crude mixture was chromatographed over silica gel using 5-10% methanol in CH₂Cl₂ with 0.5% NH₄OH, give the amide (14.3 g, 93%). The purified amide intermediate (14.3 g, 0.074 moles) was dissolved in THF (300 mL). Lithium aluminum hydride (0.148 moles, 148 mL of 1M soln. in THF, 2.0 eq.) was added and the mixture was refluxed for 3 days. The mixture was carefully quenched with 1N NaOH (10 mL) and refluxed for three hours. The hot solution was filtered over celite, and the solvent was removed to give pure N-cyclopropylmethyl-3-(1H)-imidazolylpropylamine (7.57 g, 57%) as a viscous yellow oil. NMR (CDCl₃); 0.09 (m, 2H); 0.46 (m, 2H); 0.90 (m, 1H); 1.89 (quintet, J=6.9Hz, 2H); 2.43 (d, J=6.9 Hz, 2H); 2.61 (t, J=6.8Hz, 2H); 4.05 (t, J=6.9Hz, 2H); 6.92 (s, 1H); 7.05 (s, 1H); 7.48 (s, 1H).

EXAMPLE 59**4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(N'-cyclopropylmethyl)-N'(3-(1H)-imidazolylpropyl)]-1(R)-methylpropylcarboxamido]benzenesulfonamide**

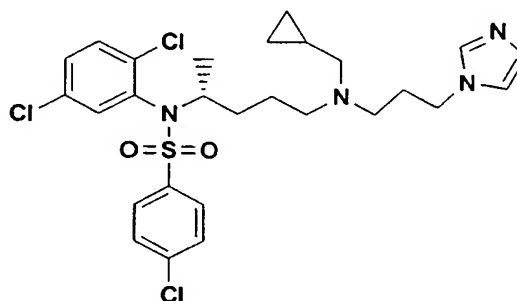
4-chloro-N-(2,5-dichlorophenyl)-N-(3-(carboxy)-1(R)-methylpropyl)benzenesulfonamide (405 mg, 0.928 mmoles) was dissolved in THF (10 mL) and CH₂Cl₂ (15 mL). N-Cyclopropylmethyl-3-(1H)-imidazolylpropylamine (166 mg, 0.928 mmoles) was added along with 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride (230 mg, 0.0012 moles, 1.3 eq.) and Hunig's base (1 drop). The mixture was stirred at room temperature for 18 hours and the solvents were removed. The residue was dissolved in CH₂Cl₂, washed with sat. NaHCO₃, and brine. The organic layer was dried over Na₂SO₄ and evaporated. Chromatography over silica gel using 2-10% methanol

in CH₂Cl₂ with 0.5% NH₄OH gave 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(N'-cyclopropylmethyl)-N'(3-(1H)-imidazolylpropyl)]-1(R)-methylpropylcarboxamido]benzenesulfonamide (370 mg, 67%). Yellow viscous oil: IR (neat, CH₂Cl₂) 1637, 1467, 1348, 1166, 1095, 622 cm⁻¹; MS (ESI+), 599 (M+H)⁺.

5

EXAMPLE 60

4-chloro-N-(2,5-dichlorophenyl)-N-[4-(N'-cyclopropylmethyl)-N'(3-(1H)-imidazolylpropylamino)-1(R)-methylbutyl]benzenesulfonamide



4-chloro-N-(2,5-dichlorophenyl)-N-(4-(N-cyclopropylmethyl-N-3-(1H)-imidazolylpropyl)-1(R)-methylbutylcarboxamide)benzenesulfonamide (1.00 g, 1.67 mmoles) was dissolved in THF (50 mL). Borane dimethyl sulfide (2.51 moles, 1.25 mL of a 2.0M solution in toluene, 1.5 eq.) was added and the mixture was refluxed for 6 hours, then allowed to stir at room temperature for 18 hours. The mixture was slowly quenched with methanol (5 mL), and 1N HCl (5mL). The solvent was removed, the residue was dissolved in CH₂Cl₂ and washed with 1N NaOH, then brine. Prep HPLC (Reverse phase, methanol/H₂O/0.1% trifluoroacetic acid) gave a small amount of pure product (75.2 mg, 8%). Yield=8%; Colorless viscous oil: IR (neat, CH₂Cl₂) 1467, 1350, 1167, 1094, 753, 622 cm⁻¹; MS (ESI+), 583 (M+H)⁺.

EXAMPLE 61

2-(methylsulfonylmethyl)piperidine 2-(methylsulfonylmethyl)pyridine

Picolyl chloride hydrochloride (15.9 g, 0.0967 moles) was dissolved in DMF (70 mL) and methanesulfinic acid sodium salt (10.9 g, 0.106 moles, 1.1 eq.) was added along with triethylamine (10.7 g, 0.106 moles, 1.1eq.). The mixture was refluxed for 1 hour. The DMF was removed, the residue dissolved in CH₂Cl₂, washed with sat. Na₂CO₃, and brine. The organic layer was dried over Na₂SO₄ and evaporated to give crude product. Purification was performed over silica gel using 20-100% ethyl acetate/hexane to give a yellow oil which solidified on standing (4.50 g, 27%).

EXAMPLE 62**(2) 2-(methanesulfonylmethyl)piperidine**

2-(Methanesulfonylmethyl)pyridine (4.40 g, 0.0257 moles) and PtO₂ (0.50 g) were suspended in ethanol (80 mL) with 1N HCl (15 mL). The mixture was hydrogenated at 50 psi for 18 hours. The catalyst was filtered and the solvent removed. The residue was dissolved in CH₂Cl₂ and washed with sat. Na₂CO₃. The aqueous layer was extracted with CH₂Cl₂ (3 x 25 mL). The organic layers were combined and dried over Na₂SO₄ and evaporated to give a yellow oil (4.11 g, 90%) which solidified on standing. Further purification was unnecessary. LCMS (178, M+H).

EXAMPLE 63**4-(methanesulfonylmethyl)piperidine**

To a stirred solution of 4-(hydroxymethyl)piperidine (6.00 g, 52.0 mmol) in 100 mL of CH₂Cl₂ was added di-*tert*-butyl dicarbonate (12.52 g, 57.0 mmol) at 0 °C and stirred for 1h. The reaction mixture was warmed to room temperature over a period of 1 h. The solvents were removed and the solid was diluted with 250 mL of ethyl acetate, washed with 1M NaOH (200 mL), brine (200 mL), and dried over Na₂SO₄. The solvent was evaporated to afford an oil.

The resulting oil was dissolved in toluene (300 mL) and triphenylphosphine (14 g, 55 mmol), iodine (14 g, 55 mmol), and imidazole (4.3 g, 63 mmol) were added. The reaction mixture was stirred at room temperature for 1h and the solvent was removed. The crude product was passed through silica gel using 10% ethyl acetate in hexanes as the eluent to yield an oil after concentration of the desired fractions.

The resulting oil was dissolved in THF (100 mL) and sodium thiomethoxide (1.20 g, 16.0 mmol) was added at room temperature. The reaction mixture was stirred for 12 h and then diluted with ethyl acetate (100 mL), washed with water (200 mL), and dried over Na₂SO₄. The solvents were removed to afford an oil.

The resulting oil was dissolved in CH₂Cl₂ and 3-chloroperoxybenzoic acid (5.90 g, 34.0 mmol) at room temperature and allowed to stir overnight. The reaction mixture was washed with 1N NaOH (50 mL), and dried over Na₂SO₄. The crude sulfone was purified using silica gel chromatography (ethyl acetate) to yield the title compound as an oil in 41% overall yield.

EXAMPLE 64**3-(methylsulfonylmethyl)piperidine**

To a stirred solution of 3-(hydroxymethyl)piperidine (4.43 g, 35.0 mmol) and pyridine (14.2 mL) in 100 mL of CH₂Cl₂ was added benzoyl chloride (4.06 mL, 35.0 mmol) at 0 °C and stirred for 18h. This mixture was washed with 2M HCl (50 mL), dried over Na₂SO₄ and the solvent was evaporated to afford an oil.

The resulting oil was dissolved in CH₂Cl₂ (70 mL), triethylamine (17.6 mL), and methanesulfonyl chloride (5.74 mL, 70.0 mmol). The reaction mixture was stirred at room temperature for 12 h. This mixture was washed with water (50 mL), dried over Na₂SO₄ and the solvent was evaporated to afford an oil.

The resulting oil was dissolved in THF (70 mL) and sodium thiomethoxide (4.48 g, 64.2 mmol) was added at room temperature. The reaction mixture was stirred for 12 h and then diluted with ethyl acetate (100 mL), washed with water (200 mL), and dried over Na₂SO₄. The solvents were removed to afford an oil.

The resulting oil was dissolved in CH₂Cl₂ (100 mL) and 80% 3-chloroperoxybenzoic acid (20.1 g, 70.0 mmol) was added at room temperature and allowed to stir overnight. The reaction mixture was washed with 1N NaOH (50 mL), and dried over Na₂SO₄. The crude sulfone was purified using silica gel chromatography (ethyl acetate) to yield an 4.69 g of an oil.

The resulting oil was suspended in 50 mL of 6N HCl and heated to 110 °C for 18h. To the resulting solution was added 35 mL of 10N NaOH and the mixture was extracted with ether (10x100mL). After evaporation of the solvent, the title compound was isolated as an oil in 30% overall yield.

EXAMPLE 65**4-(sulfonylmethyl)piperidine**

To a stirred solution of 4-(hydroxy)piperidine (3.89 g, 35.0 mmol) and pyridine (14.2 mL) in 100 mL of CH₂Cl₂ was added benzoyl chloride (4.06 mL, 35.0 mmol) at 0 °C and stirred for 18h. This mixture was washed with 2M HCl (50 mL), dried over Na₂SO₄ and the solvent was evaporated to afford an oil.

The resulting oil was dissolved in CH₂Cl₂ (70 mL), triethylamine (17.6 mL), and methanesulfonyl chloride (5.74 mL, 70.0 mmol). The reaction mixture was stirred at room temperature

for 12h. This mixture was washed with water (50 mL), dried over Na_2SO_4 and the solvent was evaporated to afford an oil.

The resulting oil was dissolved in THF (70 mL) and sodium thiomethoxide (4.48 g, 64.2 mmol) was added at room temperature. The reaction mixture was stirred for 12 h and then diluted with ethyl acetate (100 mL), washed with water (200 mL), and dried over Na_2SO_4 . The solvents were removed to afford an oil.

The resulting oil was dissolved in CH_2Cl_2 (100 mL) and 80% 3-chloroperoxybenzoic acid (20.1 g, 70.0 mmol) was added at room temperature and allowed to stir overnight. The reaction mixture was washed with 1N NaOH (50 mL), and dried over Na_2SO_4 . The crude sulfone was purified using silica gel chromatography (ethyl acetate) to yield 5.18 g of an oil.

The resulting oil was suspended in 50 mL of 6N HCl and heated to 110 °C for 18 h. To the resulting solution was added 35 mL of 10N NaOH and the mixture was extracted with ether (10x100mL). After evaporation of the solvent, the title compound was isolated as an oil in 36% overall yield.

15

EXAMPLE 66

3-(sulfonylmethyl)piperidine

To a stirred solution of 3-(hydroxy)piperidine hydrochloride (5.29 g, 35.0 mmol) and pyridine (14.2 mL) in 100 mL of CH_2Cl_2 was added benzoyl chloride (4.06 mL, 35.0 mmol) at 0 °C and stirred for 18h. This mixture was washed with 2M HCl (50 mL), dried over Na_2SO_4 and the solvent was evaporated to afford an oil.

The resulting oil was dissolved in CH_2Cl_2 (70 mL), triethylamine (17.6 mL), and methanesulfonyl chloride (5.74 mL, 70.0 mmol). The reaction mixture was stirred at room temperature for 12 h. This mixture was washed with water (50 mL), dried over Na_2SO_4 and the solvent was evaporated to afford an oil.

The resulting oil was dissolved in THF (70 mL) and sodium thiomethoxide (4.48 g, 64.2 mmol) was added at room temperature. The reaction mixture was stirred for 12 h and then diluted with ethyl acetate (100 mL), washed with water (200 mL), and dried over Na_2SO_4 . The solvents were removed to afford an oil.

The resulting oil was dissolved in CH_2Cl_2 (100 mL) and 80% 3-chloroperoxybenzoic acid (20.1 g, 70.0 mmol) was added at room temperature and allowed to stir overnight. The reaction mixture was washed with 1N NaOH (50 mL), and dried over Na_2SO_4 . The crude sulfone was purified using silica gel chromatography (ethyl acetate) to yield 5.20 g of an oil.

The resulting oil was suspended in 50 mL of 6N HCl and heated to 110 °C for 18 h. To the resulting solution was added 35 mL of 10N NaOH and the mixture was extracted with ether (10x100mL). After evaporation of the solvent, the title compound was isolated as an oil in 38% overall yield.

5

EXAMPLE 67**(S)-3-(sulfonylmethyl)pyrrolidine**

To a stirred solution of (R)-3-pyrrolidinol hydrochloride (4.76 g, 35.0 mmol) and pyridine (14.2 mL) in 100 mL of CH₂Cl₂ was added benzoyl chloride (4.06 mL, 35.0 mmol) at 0 °C and stirred for 18 h. This mixture was washed with 2M HCl (50 mL), dried over Na₂SO₄ and the solvent was evaporated to afford an oil.

The resulting oil was dissolved in CH₂Cl₂ (70 mL), triethylamine (17.6 mL), and methanesulfonyl chloride (5.74 mL, 70.0 mmol). The reaction mixture was stirred at room temperature for 12 h. This mixture was washed with water (50 mL), dried over Na₂SO₄ and the solvent was evaporated to afford an oil.

The resulting oil was dissolved in THF (70 mL) and sodium thiomethoxide (4.48 g, 64.2 mmol) was added at room temperature. The reaction mixture was stirred for 12 h and then diluted with ethyl acetate (100 mL), washed with water (200 mL), and dried over Na₂SO₄. The solvents were removed to afford an oil.

The resulting oil was dissolved in CH₂Cl₂ (100 mL) and 80% 3-chloroperoxybenzoic acid (20.1 g, 70.0 mmol) at room temperature and allowed to stir overnight. The reaction mixture was washed with 1N NaOH (50 mL), and dried over Na₂SO₄. The crude sulfone was purified using silica gel chromatography (ethyl acetate) to yield 5.49 g of an oil.

The resulting oil was suspended in 50 mL of 6N HCl and heated to 110 °C for 18h. To the resulting solution was added 35 mL of 10N NaOH and the mixture was extracted with ether (10x100mL). After evaporation of the solvent, the title compound was isolated as an oil in 39% overall yield.

EXAMPLE 68**(R)-(2-(methylsulfonyl)methyl)pyrrolidine**

N-Benzoyl-(R)-(2-(methylthio)methyl)pyrrolidine was prepared by the method of Dieter and
5 Tokles (J.A.C.S., 1987, 109, 2040-2046).

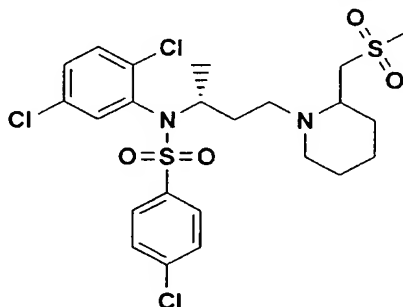
N-Benzoyl-(R)-(2-(methylthio)methyl)pyrrolidine (2.70 g, 0.0115 moles) was dissolved in
CH₂Cl₂ (50 mL), cooled to 0 °C, then meta-chloroperbenzoic acid (3.97 g, 0.0287 moles, 2.5 eq.) was
added over 10 min. The mixture was stirred at room temperature for 2 hours, diluted with CH₂Cl₂, and
washed with brine. The organic layer was dried over Na₂SO₄ and evaporated to give crude product.
10 Purification was performed over silica gel using 20-100% ethyl acetate/ hexane to give N-benzoyl-(R)-
(2-(methylsulfonyl)methyl)pyrrolidine as a yellow solid (1.70 g , 0.00637 moles, 55%). LCMS (268,
(M+H)).

N-Benzoyl-(R)-(2-(methylsulfonyl)methyl)pyrrolidine (1.70 g, 0.00637 moles) was dissolved
in 2N HCl (20 mL) and refluxed for 48 hours. The mixture was cooled and neutralized with sat.
15 K₂CO₃. The aqueous layer was extracted using 50% ethyl acetate/ t-BuOH, dried over MgSO₄, dried
over Na₂SO₄ and evaporated to give (R)-(2-(methylsulfonyl)methyl)pyrrolidine as a yellow oil (600
mg, 0.00368 moles, 58%) which was used without further purification. LCMS (186, (M+23)).

The preparation of ester intermediates can be carried out according to the general procedure
described herein for coupling of N-aryl-N-haloalkyl sulfonamides with amines, using commercially
20 available methyl thiazolidine-2-carboxylate (Lancaster, CAS# 50703-06-5). Methyl (R)-thiazolidine-4-
carboxylate (CAS#65983-36-0) was prepared from the acid following literature procedures.

EXAMPLE 69

4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidiny)-1(R)-methylpropyl)benzenesulfonamide



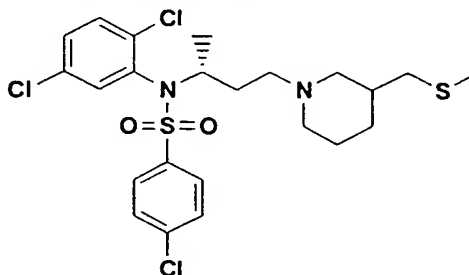
5

To a solution of 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide (0.375 mg, 0.795 mmol) in CH₃CN (20 mL), was added 2-(methylsulfonylmethyl)piperidine (0.282 g, 1.59 mmol), K₂CO₃ (500 mg), and Hunigs base (2 drops). The mixture was refluxed for 2 days. The solvent was removed and the crude mixture was dissolved in CH₂Cl₂ and washed with brine. The CH₂Cl₂ layer was dried over Na₂SO₄ and evaporated to give crude product. Purification was performed over silica gel using 10% methanol in CH₂Cl₂ with 0.5% NH₄OH to afford 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidiny)-1(R)-methylpropyl)benzenesulfonamide as a yellow glassy solid in 80% yield. IR (KBr) 1468, 1349, 1296, 1167, 1138, 1095, cm⁻¹; MS (ESI+), 567(M+H)⁺.

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EXAMPLE 70

4-chloro-N-(2,5-dichlorophenyl)-N-[3-[[3-(methylthio)methyl]-1-piperidiny]-1(R)-methylpropyl]benzenesulfonamide

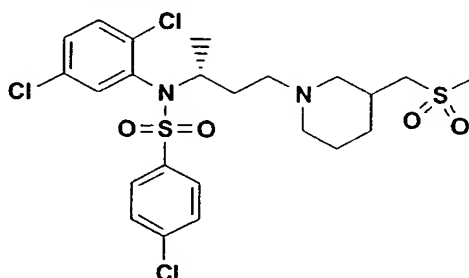


4-chloro-N-(2,5-dichlorophenyl)-N-[3-[[3-(methylthio)methyl]-1-piperidiny]-1(R)-methylpropyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidiny)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-

chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 3-(methylthiomethyl)piperidine. Yield=86%; MS (ESI+), 535(M+H)⁺.

EXAMPLE 71

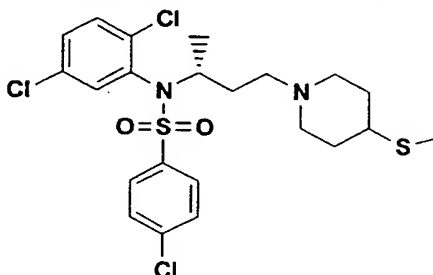
4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-(methylsulfonyl)methyl)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide



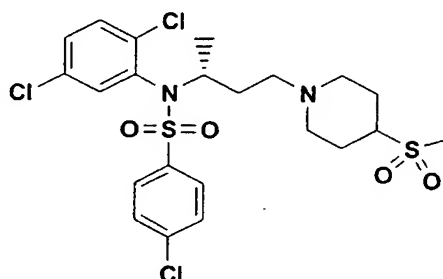
4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-(methylsulfonyl)methyl)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 3-(methylsulfonylmethyl)piperidine. Yield=81%; MS (ESI+), 567(M+H)⁺.

EXAMPLE 72

4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(4-methylthio)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide

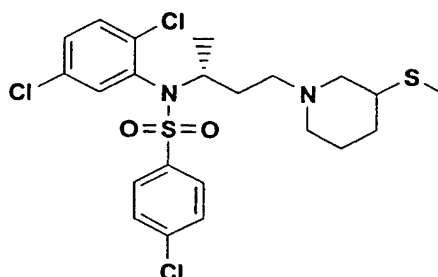


4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(4-methylthio)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 4-(methylthio)-piperidine. Yield=88%; MS (ESI+), 521(M+H)⁺.

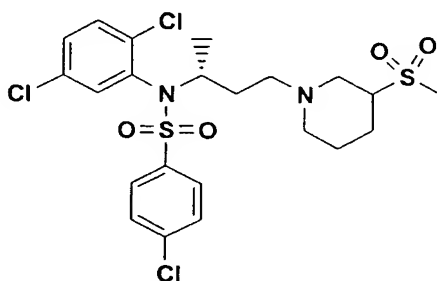
EXAMPLE 73**4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide**

- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylpropyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 4-(methylsulfonyl)-piperidine. Yield=94%; MS (ESI+), 553(M+H)⁺.

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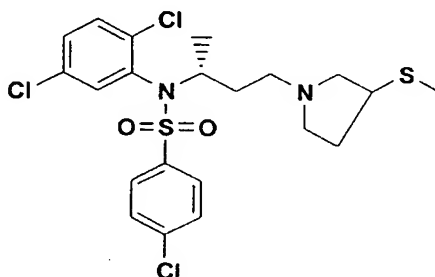
EXAMPLE 74**4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylthio)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide**

- 15 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylthio)-1-piperidinyl]-1(R)-methylpropyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 3-(methylthio)-piperidine. Yield=85%; MS (ESI+), 521(M+H)⁺.

EXAMPLE 75**4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylsulfonyl)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide**

5 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylsulfonyl)-1-piperidinyl]-1(R)-methylpropyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 3-(methylsulfonyl)-piperidine. Yield=90%; MS (ESI+), 553(M+H)⁺.

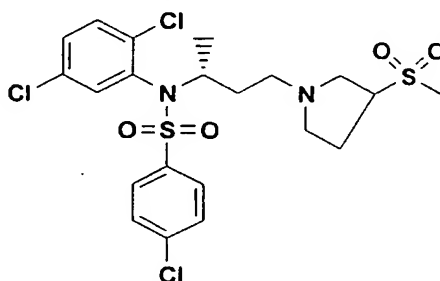
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EXAMPLE 76**4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylthio)-1-pyrrolidinyl]-1(R)-methylpropyl]benzenesulfonamide**

15 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylthio)-1-pyrrolidinyl]-1(R)-methylpropyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 3-(methylthio)pyrrolidine. Yield=83%; MS (ESI+), 507(M+H)⁺.

EXAMPLE 77

4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylpropyl]benzenesulfonamide

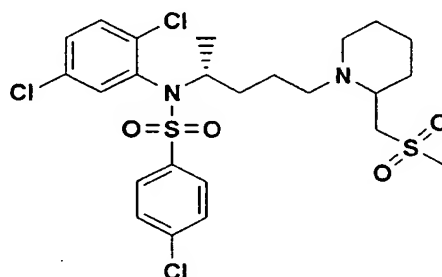


- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylpropyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 3-(methylsulfonyl)-pyrrolidine. Yield=86%; MS (ESI+), 539(M+H)⁺.

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EXAMPLE 78

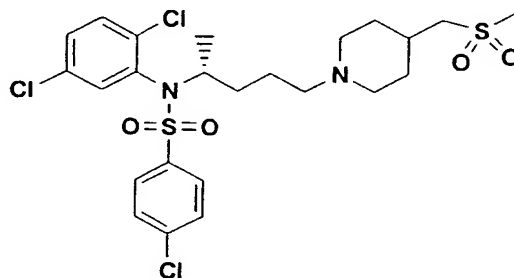
4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylbutyl)benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[2-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 2-(methylsulfonyl-methyl)piperidine. Yield=28 %; yellow foam: IR (neat, CH₂Cl₂) 1467, 1296, 1166, 1138, 1095, 622, cm⁻¹; MS (ESI+), 581(M+H)⁺.

EXAMPLE 79

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[4-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide

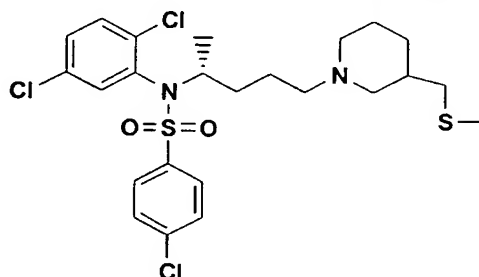


- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[4-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 4-(methylsulfonyl)methylpiperidine. Yield=60%; MS (ESI+), 581(M+H)⁺.

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EXAMPLE 80

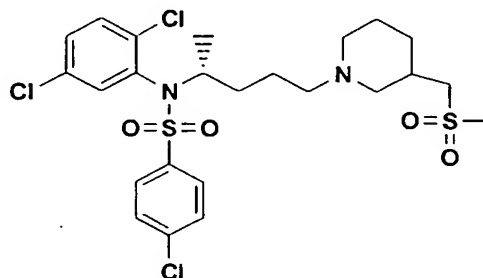
4-chloro-N-(2,5-dichlorophenyl)-N-[4-[3-[(methylthio)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[3-[(methylthio)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 3-(methylthio)methylpiperidine. Yield=91%; MS (ESI+), 549(M+H)⁺.

EXAMPLE 81

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[3-[(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide

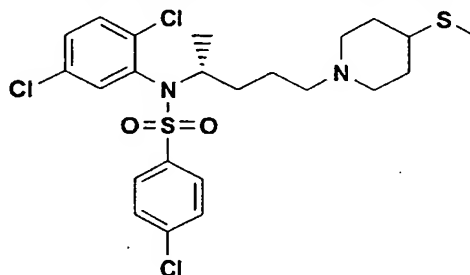


5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[3-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 3-(methylsulfonylmethyl)piperidine. Yield=77%; MS (ESI+), 581(M+H)⁺.

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EXAMPLE 82

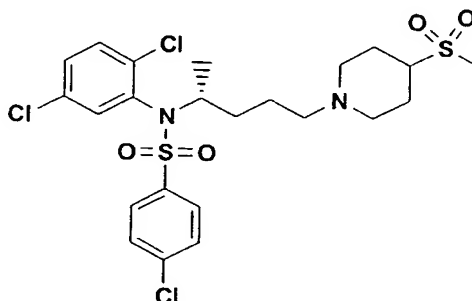
4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(4-methylthio)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide



15 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(4-methylthio)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 4-(methylthio)piperidine. Yield=88%; MS (ESI+), 535(M+H)⁺.

EXAMPLE 83

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide

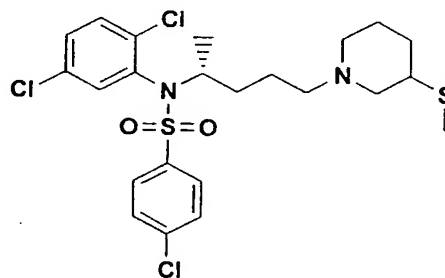


- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 4-(methylsulfonyl)-piperidine. Yield=92%; MS (ESI+), 567(M+H)⁺.

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EXAMPLE 84

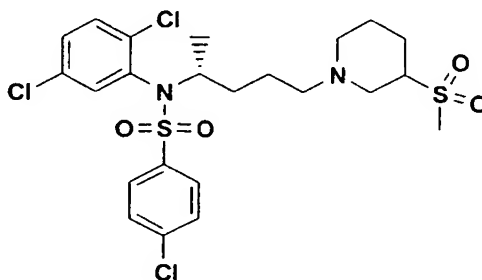
4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylthio)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylthio)-1-piperidinyl]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 3-(methylthio)piperidine. Yield=89%; MS (ESI+), 535(M+H)⁺.

EXAMPLE 85

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylsulfonyl)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide

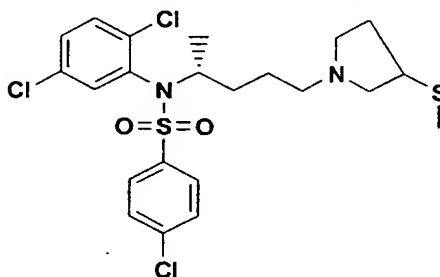


- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylsulfonyl)-1-piperidinyl]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 3-(methylsulfonyl)-piperidine. Yield=93%; MS (ESI+), 567(M+H)⁺.

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EXAMPLE 86

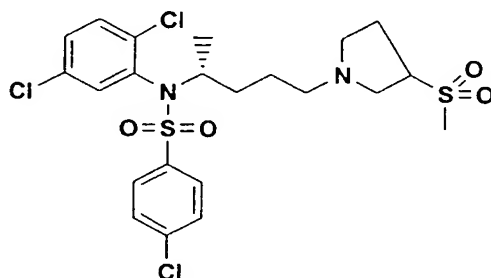
4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylthio)-1-pyrrolidinyl]-1(R)-methylbutyl]benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylthio)-1-pyrrolidinyl]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 3-(methylthio)-pyrrolidine. Yield=86%; MS (ESI+), 521(M+H)⁺.

EXAMPLE 87

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylbutyl]benzenesulfonamide

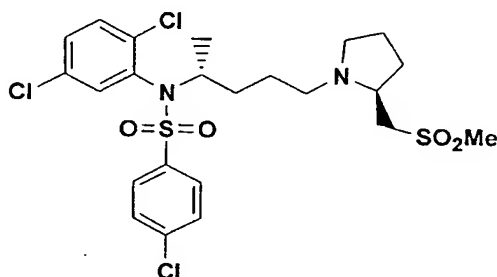


- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 3-(methylsulfonyl)-pyrrolidine. Yield=88%; MS (ESI+), 553(M+H)⁺.

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EXAMPLE 88

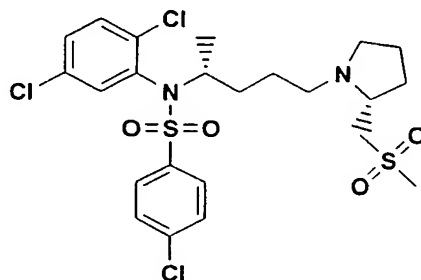
4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-(((R)-methylsulfonyl)methyl)-1-pyrrolidinyl)-1(R)-methylbutyl)benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-(((R)-methylsulfonyl)methyl)-1-pyrrolidinyl)-1(R)-methylbutyl)benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with (R)-(2-(methylsulfonyl)methyl)pyrrolidine. Yield=10 %; yellow oil: IR (neat, CH₂Cl₂) 1349, 1301, 1166, 1130, 1094, 622, cm⁻¹; MS (ESI+), 569(M+H)⁺.

EXAMPLE 89

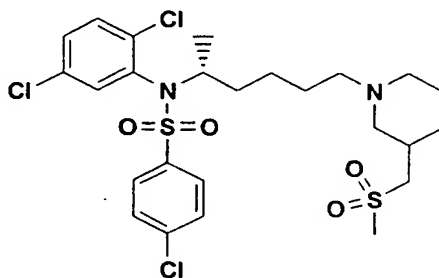
4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-(((S)-methylsulfonyl)methyl)-1-pyrrolidiny)-1(R)-methylbutyl)benzenesulfonamide



- 5 4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-(((S)-methylsulfonyl)methyl)-1-pyrrolidiny)-1(R)-methylbutyl)benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidiny)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with (S)-(2-(methylsulfonyl)methyl)pyrrolidine. Yield=43 %; yellow oil: IR (neat, CH₂Cl₂) 1467, 1350, 1302, 1167,
10 1094, 622, cm⁻¹; MS (ESI+), 569(M+H)⁺.

EXAMPLE 90

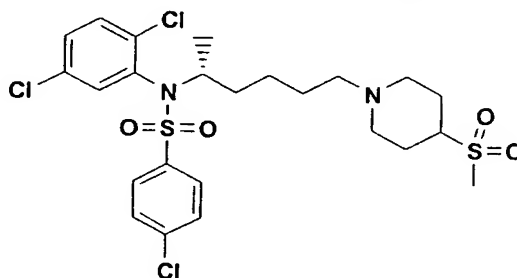
4-chloro-N-(2,5-dichlorophenyl)-N-[5-[3-[(methylsulfonyl)methyl]-1-piperidiny]-1(R)-methylpentyl]benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[[3-(methylsulfonyl)methyl]-1-piperidiny]-1(R)-methylpentyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidiny)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-5-bromopentyl]benzenesulfonamide with 3-(methylsulfonylmethyl)piperidine. Yield=74%; MS (ESI+), 595(M+H)⁺.

EXAMPLE 91

4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylpentyl]benzenesulfonamide

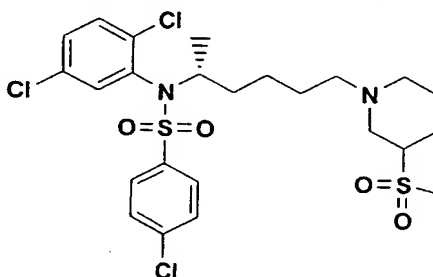


- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylpentyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-5-bromopentyl]benzenesulfonamide with 4-(methylsulfonyl)-piperidine. Yield=79%; MS (ESI+), 581(M+H)⁺.

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EXAMPLE 92

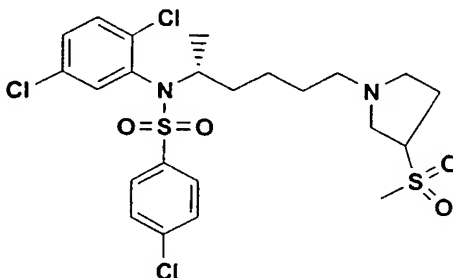
4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(3-methylsulfonyl)-1-piperidinyl]-1(R)-methylpentyl]benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(3-methylthiosulfonyl)-1-piperidinyl]-1(R)-methyl-pentyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-5-bromopentyl]benzenesulfonamide with 3-(methylsulfonyl)-piperidine. Yield=82%; MS (ESI+), 581(M+H)⁺.

EXAMPLE 93

4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylpentyl]benzenesulfonamide

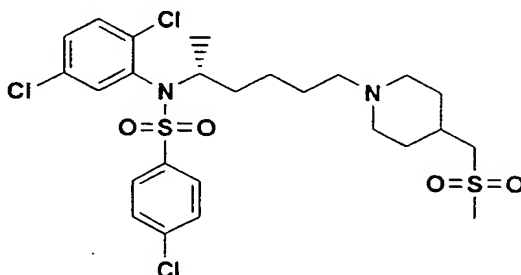


5 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylpentyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-5-bromopentyl]benzenesulfonamide with 3-(methylsulfonyl)-pyrrolidine. Yield=72%; MS (ESI+), 567(M+H)⁺.

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EXAMPLE 94

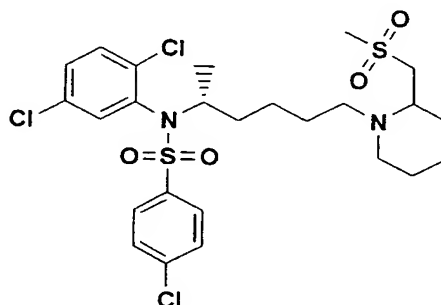
4-chloro-N-(2,5-dichlorophenyl)-N-(5-(4-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpentyl)benzenesulfonamide



15 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[[4-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylpentyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-5-bromopentyl]benzenesulfonamide with 4-(methylsulfonylmethyl)piperidine. Yield=68%; yellow oil: IR (neat, CH₂Cl₂) 1467, 1301, 1166, 1136, 1093, 622 cm⁻¹; MS (ESI+), 595(M+H)⁺.

EXAMPLE 95

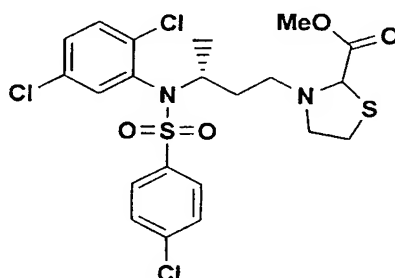
4-chloro-N-(2,5-dichlorophenyl)-N-(5-(2-((methylsulfonyl)methyl)-1-piperidiny)-1(R)-methylpentyl)benzenesulfonamide



- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[[2-(methylsulfonyl)methyl]-1-piperidiny]-1(R)-methylpentyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidiny)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-5-bromopentyl]benzenesulfonamide with 2-(methylsulfonylmethyl)piperidine. Yield=73 %; yellow oil: IR (neat, CH₂Cl₂) 1467, 1297, 1166, 1139, 1094,
10 623, cm⁻¹; MS (ESI+), 595(M+H)⁺.

EXAMPLE 96

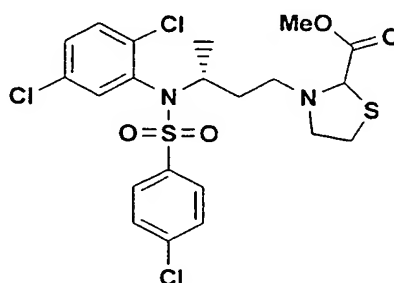
4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxymethyl-3-thiazolidiny)-1(R)-methylpropyl)benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxymethyl-3-thiazolidiny)-1(R)-methylpropyl)-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidiny)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 2-carboxymethyl-3-thiazolidine. Yield=6%; White powder: IR (KBr) 1747, 1467, 1352, 1166, 1094, 622 cm⁻¹; MS
20 (ESI+), 537 (M+H)⁺.

EXAMPLE 97

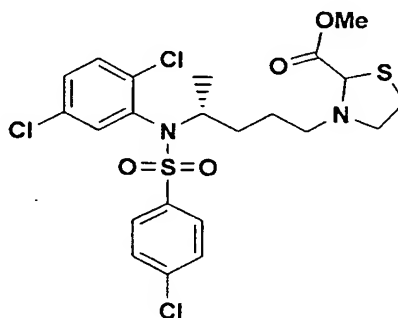
4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide



- 5 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylpropyl)-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 2-carboxymethyl-3-thiazolidine. Yield=7%; White powder: IR (KBr) 1747, 1467, 1352, 1167, 1094, 622 cm^{-1} ; MS
- 10 (ESI+), 537(M+H)⁺.

EXAMPLE 98

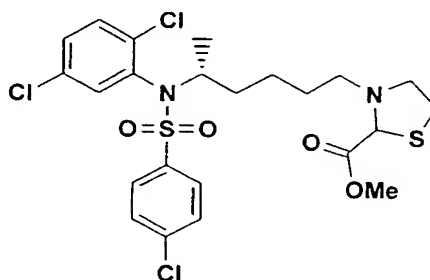
4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylbutyl)benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylbutyl)-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with 2-carboxymethyl-3-thiazolidine. Yield=25%; MS (ESI+), 551(M+H)⁺.

EXAMPLE 99

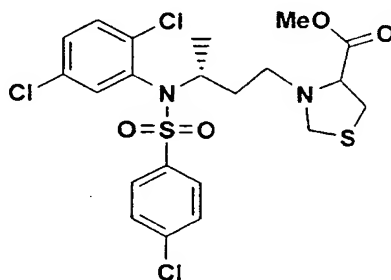
4-chloro-N-(2,5-dichlorophenyl)-N-(5-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylpentyl)benzenesulfonamide



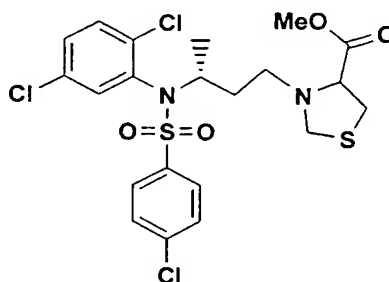
- 5 4-chloro-N-(2,5-dichlorophenyl)-N-(5-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylpentyl)-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-5-bromopentyl]benzenesulfonamide with 2-carboxymethyl-3-thiazolidine. Yield=39%; Colorless oil: IR (neat, CH₂Cl₂) 1748, 1467, 1352, 1167, 1095, 623 cm⁻¹;
- 10 MS (ESI⁺), 565(M+H)⁺.

EXAMPLE 100

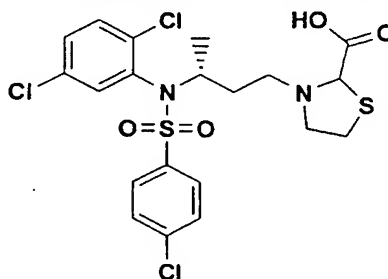
4-chloro-N-(2,5-dichlorophenyl)-N-(3-(5-carboxymethyl-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide -



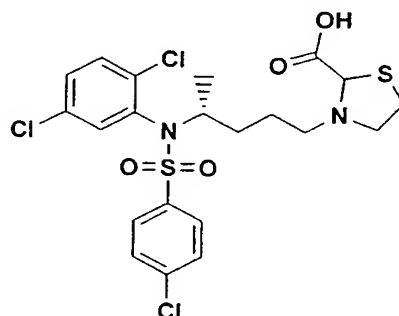
- 15 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(5-carboxymethyl-3-thiazolidinyl)-1(R)-methylpropyl)-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 5-carboxymethyl-3-thiazolidine. Yield=31%; Colorless oil: IR (neat, CH₂Cl₂) 1742, 1467, 1352, 1167, 1094, 622 cm⁻¹;
- 20 MS (ESI⁺), 539 (M+H)⁺.

EXAMPLE 101**4-chloro-N-(2,5-dichlorophenyl)-N-(3-(5-carboxymethyl-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide**

- 5 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(5-carboxymethyl-3-thiazolidinyl)-1(R)-methylpropyl)-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-((methylsulfonyl)methyl)-1-piperidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-3-bromopropyl]benzenesulfonamide with 5-carboxymethyl-3-thiazolidine. Yield=21%; Colorless oil: IR (neat, CH₂Cl₂) 1738, 1467, 1351, 1167, 1095, 622 cm⁻¹;
10 MS (ESI+), 539 (M+H)⁺.

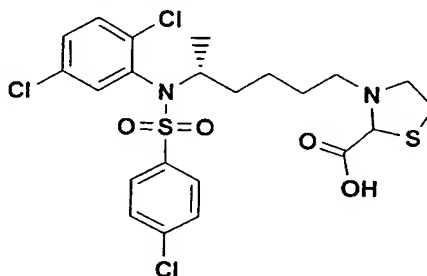
EXAMPLE 102**4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide**

- 15 To a stirring solution of 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide (109 mg, 0.203 mmol) in methanol (20 mL) was added 50% aqueous KOH (1.0 mL) and the mixture was stirred at room temperature for 18 hours. The solvent was removed and the crude mixture was dissolved in CH₂Cl₂ and washed with 1N HCl. The CH₂Cl₂ layer was dried over Na₂SO₄ and evaporated to give crude product. Purification was
20 performed over silica gel using 5-10% methanol in CH₂Cl₂ with 0.5% NH₄OH to afford 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide as a beige foam in 66% yield. IR (KBr) 1467, 1351, 1167, 1094, 753, 622 cm⁻¹; MS (ESI+), 523 (M+H)⁺.

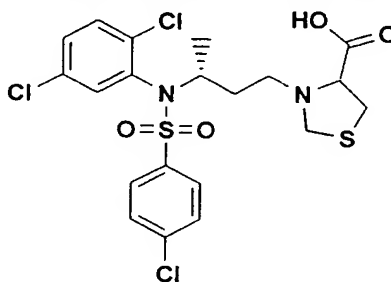
EXAMPLE 103**4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-carboxy-3-thiazolidinyl)-1(R)-methylbutyl)benzenesulfonamide**

- 5 4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-carboxy-3-thiazolidinyl)-1(R)-methylbutyl)benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-(2,5-dichlorophenyl)-N-(4-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylbutyl)benzenesulfonamide with 50% aqueous KOH. Yield=77%; White foam: IR (KBr) 1467, 1351, 1167, 1093, 753, 622 cm^{-1} ; MS (ESI+), 537 (M+H)⁺.

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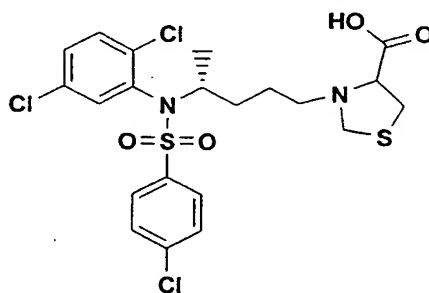
EXAMPLE 104**4-chloro-N-(2,5-dichlorophenyl)-N-(5-(2-carboxy-3-thiazolidinyl)-1(R)-methylpentyl)benzenesulfonamide**

- 15 4-chloro-N-(2,5-dichlorophenyl)-N-(5-(2-carboxy-3-thiazolidinyl)-1(R)-methylpentyl)benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-(2,5-dichlorophenyl)-N-(5-(2-carboxymethyl-3-thiazolidinyl)-1(R)-methylpentyl)benzenesulfonamide with 50% aqueous KOH. Yield=67%; White foam: IR (neat, CH_2Cl_2) 1467, 1350, 1167, 1093, 753, 622 cm^{-1} ; MS (ESI+), 553 (M+H)⁺.

EXAMPLE 105**4-chloro-N-(2,5-dichlorophenyl)-N-(3-(5-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide**

5 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(5-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(5-carboxymethyl-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide with 50% aqueous KOH. Yield=70%; White foam: IR (KBr) 1467, 1350, 1167, 1094, 753, 622 cm^{-1} ; MS (ESI+), 525 (M+H)⁺.

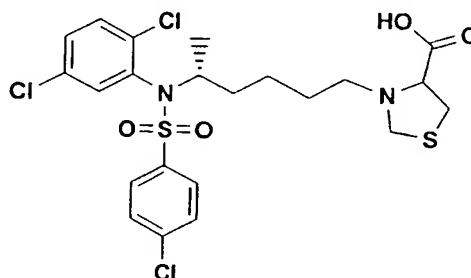
10

EXAMPLE 106**4-chloro-N-(2,5-dichlorophenyl)-N-(4-(5-carboxy-3-thiazolidinyl)-1(R)-methylbutyl)benzenesulfonamide**

15 4-chloro-N-(2,5-dichlorophenyl)-N-(4-(5-carboxy-3-thiazolidinyl)-1(R)-methylbutyl)benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-(2,5-dichlorophenyl)-N-(4-(5-carboxymethyl-3-thiazolidinyl)-1(R)-methylbutyl)benzenesulfonamide with 50% aqueous KOH. Yield=45%; White powder: IR (KBr) 1467, 1350, 1167, 1094, 754, 622 cm^{-1} ; MS (ESI+), 537 (M+H)⁺.

EXAMPLE 107

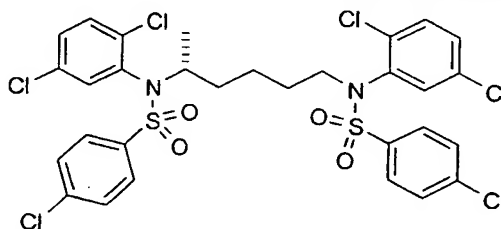
4-chloro-N-(2,5-dichlorophenyl)-N-(5-(5-carboxy-3-thiazolidinyl)-1(R)-methylpentyl)benzenesulfonamide



5 4-chloro-N-(2,5-dichlorophenyl)-N-(5-(5-carboxy-3-thiazolidinyl)-1(R)-methylpentyl)benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-(3-(2-carboxy-3-thiazolidinyl)-1(R)-methylpropyl)benzenesulfonamide by reacting 4-chloro-N-(2,5-dichlorophenyl)-N-(5-(5-carboxymethyl-3-thiazolidinyl)-1(R)-methylpentyl)benzenesulfonamide with 50% aqueous KOH. Yield=34%; White powder: IR (KBr) 1467, 1350, 1167, 1094, 754, 623 cm^{-1} ; MS (ESI+), 551
10 (M+H)⁺.

EXAMPLE 108

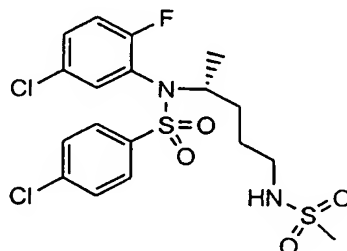
4-chloro-N-(2,5-dichlorophenyl)-N-[5-[N-(2,5-dichlorophenyl)-N-[(4-chlorophenyl)sulfonyl]amino]-1(R)-methylpentyl]benzenesulfonamide



15 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[N-(2,5-dichlorophenyl)-N-[(4-chlorophenyl)sulfonyl]amino]-1(R)-methylpentyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[4-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-(2,5-dichlorophenyl)-N-[4-bromo-1(R)-methylbutyl]benzenesulfonamide with 4-chloro-N-(2,5-dichlorophenyl) benzenesulfonamide. Yield=20%; MS (ESI+),
20 771(M+NH₃)⁺.

EXAMPLE 109

4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(methylsulfonyl)amino]-1(R)-methylbutyl]benzenesulfonamide

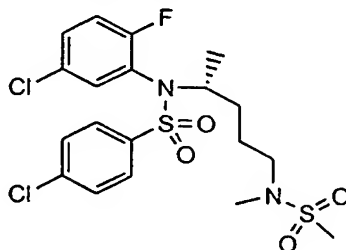


5 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(methylsulfonyl)amino]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[4-(methylsulfonyl)methyl]-1-piperidiny]-1(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-bromo-1(R)-methylbutyl]benzenesulfonamide with methane-sulfonamide. Yield=89%; MS (ESI+), 483(M+H)⁺.

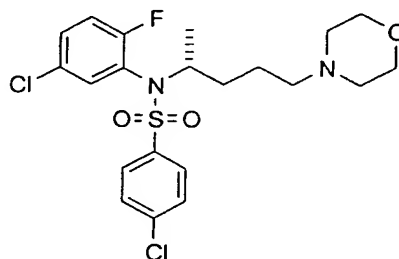
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EXAMPLE 110

4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(methylsulfonyl)methylamino]-1(R)-methylbutyl]benzenesulfonamide

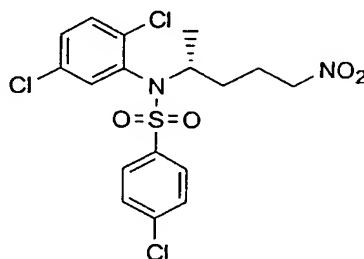


15 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(methylsulfonyl)methylamino]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[4-(methylsulfonyl)methyl]-1-piperidiny]-1(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-bromo-1(R)-methylbutyl]benzenesulfonamide with N-methyl-methanesulfonamide. Yield=81%; MS (ESI+), 497(M+H)⁺.

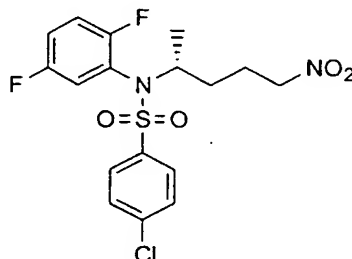
EXAMPLE 111**4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-(4-morpholinyl)-1(R)-methylbutyl]benzenesulfonamide**

- 5 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-(morpholinyl)-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[4-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-bromo-1(R)-methylbutyl]benzenesulfonamide with morpholine. Yield=87%; MS (ESI+), 475(M+H)⁺.

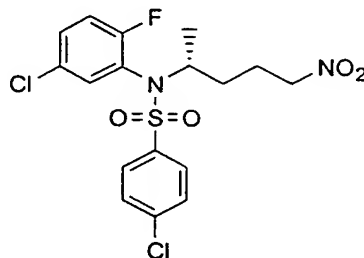
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EXAMPLE 112**4-chloro-N-(2,5-dichlorophenyl)-N-[4-nitro-1(R)-methylbutyl]benzenesulfonamide**

- To a solution of 4-chloro-n-(2,5-dichlorophenyl)-n-[(r)-1-methyl-4-bromobutyl]benzenesulfonamide (0.216 g, 0.444 mmol) in ether (4 mL) was added AgNO₂ (0.410 g, 2.67 mmol) at 22 °C.
- 15 The resulting mixture was allowed to stir at 22 °C for 4 days and the mixture was filtered and concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) of the concentrate afforded 0.129 g of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-4-nitrobutyl]benzenesulfonamide as a light brown oil in 64% yield. MS (ESI) 451.1 (m+h).

EXAMPLE 113**4-chloro-N-(2,5-difluorophenyl)-N-[4-nitro-1(R)-methylbutyl]benzenesulfonamide**

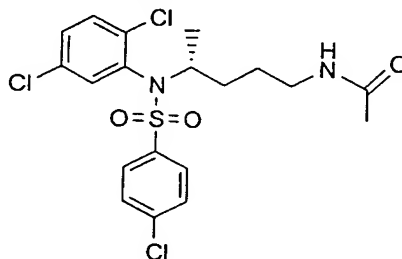
To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide (0.194 g, 0.427 mmol) in ether (4 mL) was added AgNO₂ (0.395 g, 2.56 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for 4 days. The mixture was filtered and concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) of the concentrate afforded 0.0913 g of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-nitrobutyl]benzenesulfonamide as a light brown oil in 50% yield. MS (ESI) 419.1 (M+H).

EXAMPLE 114**4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-nitro-1(R)-methylbutyl]benzenesulfonamide**

To a solution of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide (0.150 g, 0.320 mmol) in ether (4 mL) was added AgNO₂ (0.296 g, 1.92 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for 4 days. The mixture was filtered and concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) of the concentrate afforded 0.0746 g of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-4-nitrobutyl]benzenesulfonamide as a light brown oil in 53% yield. MS (ESI) 435.1 (M+H).

EXAMPLE 115

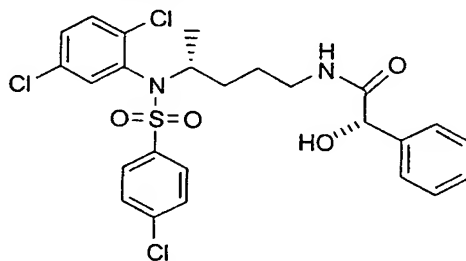
4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetylamino)butyl] benzenesulfonamide



To a solution of 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-aminobutyl]benzene-
 5 sulfonamide (35.0 mg, 0.083 mmol) in CH₂Cl₂ (2 mL) was added acetic anhydride (0.024 mL, 0.249 mmol) and pyridine (0.027 mL, 0.332 mmol) at 0 °C. The resulting mixture was allowed to stir at 22 °C overnight. To the reaction was added sat. sodium bicarbonate (20 mL). The product was extracted with CH₂Cl₂ (2 x 20mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Silica
 10 gel chromatography (1:4 ethyl acetate:hexanes) of the concentrate afforded 37.8 mg of 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetylamino)butyl]benzenesulfonamide as a colorless oil in 98% yield. MS (ESI) 463 (M+H).

EXAMPLE 116

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(S)hydroxy]phenylmethyl]carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide

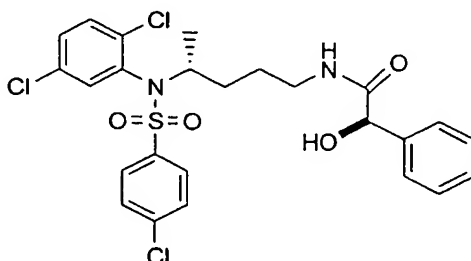


15

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(S)hydroxy]phenylmethyl]carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetylamino)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-aminobutyl]benzenesulfonamide with (S)-O-acetyl-mandelic chloride. Yield=64%; MS
 20 (ESI+), 555(M+H)⁺.

EXAMPLE 117

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(R)hydroxy]phenylmethyl]carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide

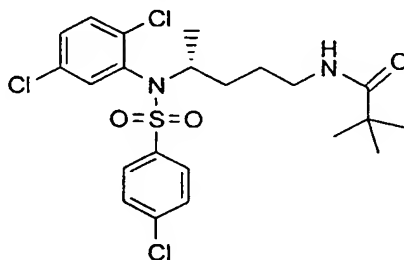


- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(R)hydroxy]phenylmethyl]carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetylamino)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[R]-1-methyl-4-aminobutyl]benzenesulfonamide with (R)-O-acetyl-mandelic chloride. Yield=57%; MS (ESI+), 555(M+H)⁺.

10

EXAMPLE 118

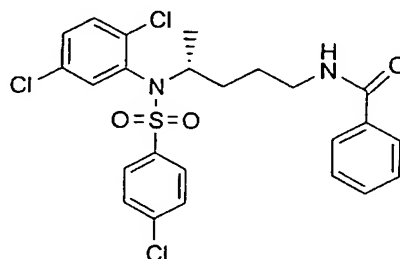
4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(1,1-dimethylethyl)carbonyl]amino]-1-methylbutyl]benzenesulfonamide



- 15 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(1,1-dimethylethyl)carbonyl]amino]-1-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetylamino)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[R]-1-methyl-4-aminobutyl]benzenesulfonamide with pivaloyl chloride. Yield=86%; MS (ESI+), 505(M+H)⁺.

EXAMPLE 119

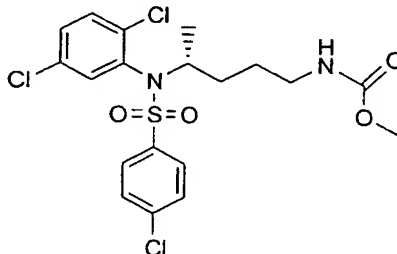
4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(phenyl)carbonyl]amino]-1-methylbutyl]benzenesulfonamide



- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(phenyl)carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetyl-amino)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[R]-1-methyl-4-aminobutyl]benzenesulfonamide with benzoyl chloride. Yield=84%; MS (ESI+), 525(M+H)⁺.

EXAMPLE 120

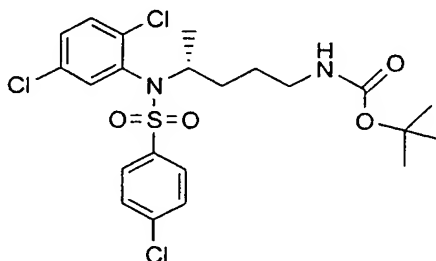
4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(methoxy)carbonyl]amino]-1-methylbutyl]benzenesulfonamide



- 10 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(methoxy)carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetyl-amino)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[R]-1-methyl-4-aminobutyl]benzenesulfonamide with methyl chloroformate. Yield=96%; MS (ESI+), 479(M+H)⁺.
- 15

EXAMPLE 121

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(1,1-dimethylethoxy)carbonyl]amino]-1-methylbutyl]benzenesulfonamide

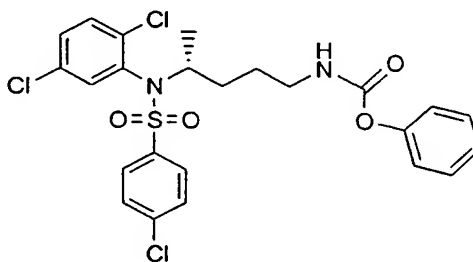


5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(1,1-dimethylethoxy)phenylmethyl]carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetyl amino)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[R]-1-methyl-4-aminobutyl]benzenesulfonamide with di-tert-butyl dicarbonate. Yield=91%; MS (ESI+), 521(M+H)⁺.

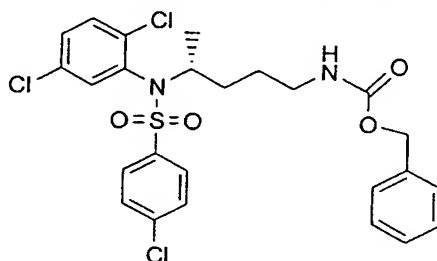
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EXAMPLE 122

4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(phenoxy)carbonyl]amino]-1-methylbutyl]benzenesulfonamide



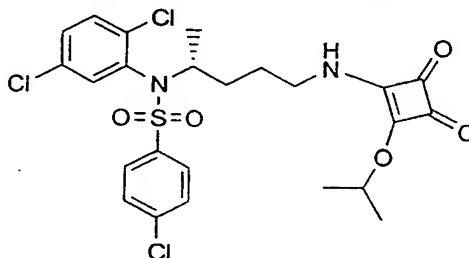
15 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(phenoxy)carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetyl amino)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[R]-1-methyl-4-aminobutyl]benzenesulfonamide with phenyl chloroformate. Yield=82%; MS (ESI+), 541(M+H)⁺.

EXAMPLE 123**4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(benzyloxy)carbonyl]amino]-1-methylbutyl]benzenesulfonamide**

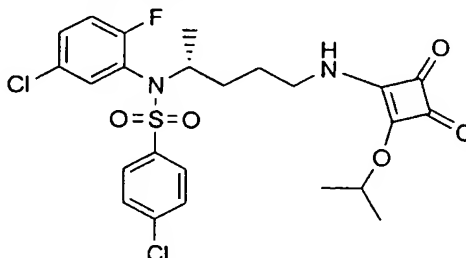
- 5 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(benzyloxy)carbonyl]amino]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-(acetyl-amino)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[R]-1-methyl-4-aminobutyl]benzenesulfonamide with benzyl chloroformate. Yield=81%; MS (ESI+), 555(M+H)⁺.

EXAMPLE 124

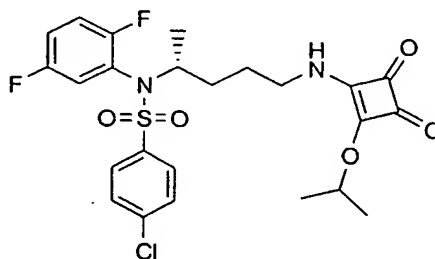
- 10 **4-chloro-N-(2,5-dichlorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide**



- 15 To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-4-aminobutyl]benzenesulfonamide (0.207 g, 0.463 mmol) in THF (3 mL) was added 3,4-diisopropoxy-3-cyclobutene-1,2-dione (0.0963 g, 0.486 mmol) dissolved in THF (2 mL) at 22 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 22 °C for 12 h. The mixture was concentrated under reduced pressure. Silica gel chromatography (3:7 ethyl acetate:hexanes) of the concentrate afforded 0.135 g of 4-chloro-N-(2,5-dichlorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide as a white solid in 50% yield. MS (ESI) 559.2 (M+H).

EXAMPLE 125**4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide**

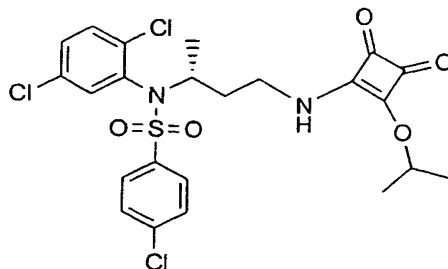
5 To a solution of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-4-aminobutyl]-benzenesulfonamide (0.185 g, 0.455 mmol) in THF (4 mL) was added 3,4-diisopropoxy-3-cyclobutene-1,2-dione (0.0948 g, 0.478 mmol) dissolved in THF (2 mL) at 22 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 22 °C for 12 h. The mixture was concentrated under reduced pressure. Silica gel chromatography (3:7 ethyl acetate:hexanes) of the concentrate afforded 0.182 g of
10 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide as a white solid in 74% yield. MS (ESI) 543.2 (M+H).

EXAMPLE 126**4-chloro-N-(2,5-difluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide**

15 To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-aminobutyl]benzenesulfonamide (0.243 g, 0.635 mmol) in THF (7 mL) was added 3,4-diisopropoxy-3-cyclobutene-1,2-dione (0.138 g, 0.698 mmol) dissolved in THF (3 mL) at 22 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 22 °C for 12 h. The mixture was concentrated under reduced
20 pressure. Silica gel chromatography (3:7 ethyl acetate:hexanes) of the concentrate afforded 0.135 g of 4-chloro-N-(2,5-difluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide as a white solid in 47% yield. MS (ESI) 527.2 (M+H).

EXAMPLE 127

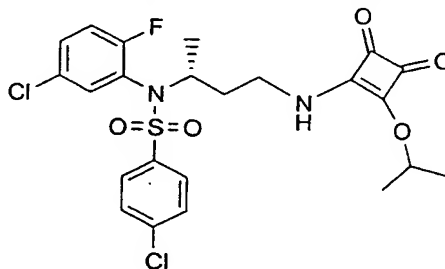
4-chloro-N-(2,5-dichlorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide



5 To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide (0.328 g, 0.805 mmol) in THF (6 mL) was added 3,4-diisopropoxy-3-cyclobutene-1,2-dione (0.176 g, 0.885 mmol) dissolved in THF (2 mL) at 22 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 22 °C for 12 h. The mixture was concentrated under reduced pressure. Silica gel chromatography (3:7 ethyl acetate:hexanes) of the concentrate afforded 0.185 g of
10 4-chloro-N-(2,5-dichlorophenyl)-N-[3-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzene-sulfonamide as a white solid in 80% yield. MS (ESI) 545 (M+H).

EXAMPLE 128

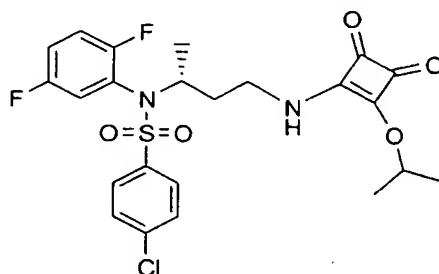
4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide



15 To a solution of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide (0.389 g, 0.995 mmol) in THF (7 mL) was added 3,4-diisopropoxy-3-cyclobutene-1,2-dione (0.217 g, 1.09 mmol) dissolved in THF (3 mL) at 22 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 22 °C for 12 h. The mixture was concentrated under reduced
20 pressure. Silica gel chromatography (3:7 ethyl acetate:hexanes) of the concentrate afforded 0.243 g of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[3-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide as a white solid in 46% yield. MS (ESI) 529.1 (M+H).

EXAMPLE 129

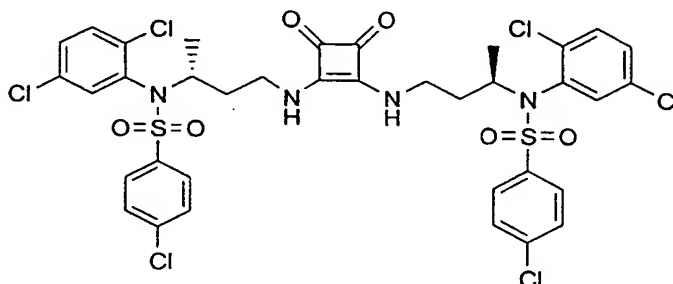
4-chloro-N-(2,5-difluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide



5 To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-3-aminopropyl]benzenesulfonamide (0.401 g, 1.07 mmol) in THF (6 mL) was added 3,4-diisopropoxy-3-cyclobutene-1,2-dione (0.233 g, 1.18 mmol) dissolved in THF (4 mL) at 22 °C under nitrogen atmosphere. The resulting mixture was allowed to stir at 22 °C for 12 h. The mixture was concentrated under reduced pressure. Silica gel chromatography (3:7 ethyl acetate:hexanes) of the concentrate afforded 0.392 g of 4-chloro-
10 N-(2,5-difluorophenyl)-N-[3-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide as a white solid in 71% yield. MS (ESI) 513.1 (M+H).

EXAMPLE 130

4-chloro-N-(2,5-dichlorophenyl)-N-[3-[2-[4-chloro-N-(2,5-dichlorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-1-cyclobutenyl]amine-1(R)-methylpropyl]benzenesulfonamide

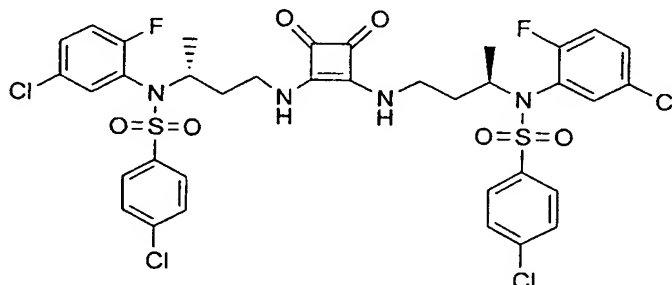


15 To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl-4-aminobutyl]benzenesulfonamide (0.125 g, 0.367 mmol) in methanol (3.0 mL) was added 4-chloro-N-(2,5-dichlorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide (0.167 g, 0.306 mmol) at 22 °C. The resulting mixture was heated to reflux for 12 hours. The desired compound precipitated while the mixture cooled to 22 °C. The mixture was filtered, washed with ethyl acetate (4 mL X 2), and dried under reduced pressure to afford 0.140 g of 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[2-[4-chloro-N-(2,5-dichlorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-

1-cyclobutenyl]amine-1(R)-methylpropyl]benzenesulfonamide as a white solid in 52% yield. MS (ESI) 893.1 (M+H).

EXAMPLE 131

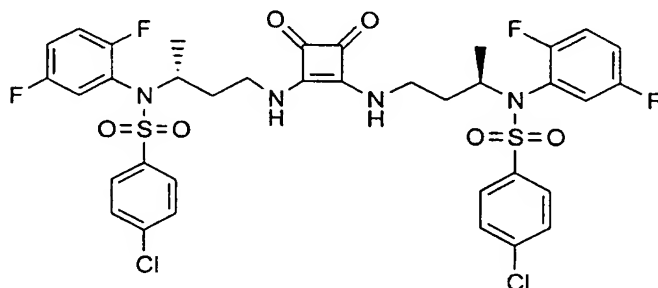
4-chloro-N-(5-chloro-2-fluorophenyl)-N-[3-[2-[4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-1-cyclobutenyl]amine-1(R)-methylpropyl]benzenesulfonamide



To a solution of 4-chloro-N-(5-fluoro-2-chlorophenyl)-N-[(R)-1-methyl-4-aminobutyl]-benzenesulfonamide (0.189 g, 0.483 mmol) in methanol (4.0 mL) was added 4-chloro-N-(5-fluoro-2-chlorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)-amine-1(R)-methylpropyl]benzenesulfonamide (0.214 g, 0.403 mmol) at 22 °C. The resulting mixture was heated to reflux for 12 hours. The desired compound precipitated while the mixture cooled to 22 °C. The mixture was filtered, washed with ethyl acetate (4 mL X 2), and dried under reduced pressure to afford 0.174 g of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[3-[2-[4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-1-cyclobutenyl]amine-1(R)-methylpropyl]benzenesulfonamide as a white solid in 50% yield. MS (ESI) 861.1 (M+H).

EXAMPLE 132

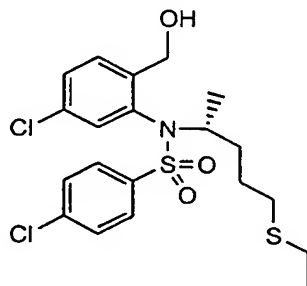
4-chloro-N-(2,5-difluorophenyl)-N-[3-[2-[4-chloro-N-(2,5-difluorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-1-cyclobutenyl]amine-1(R)-methylpropyl]benzenesulfonamide



To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-4-aminobutyl]-benzenesulfonamide (0.140 g, 0.374 mmol) in methanol (3.0 mL) was added 4-chloro-N-(2,5-difluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide (0.159 g, 0.311 mmol) at 22 °C. The resulting mixture was heated at reflux to 12 hours. The desired compound precipitated while the mixture cooled to 22 °C. The mixture was filtered, washed with ethyl acetate (3 mL X 2), and dried under reduced pressure to afford 0.124 g of 4-chloro-N-(2,5-difluorophenyl)-N-[3-[2-[4-chloro-N-(2,5-difluorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-1-cyclobutenyl]amine-1(R)-methylpropyl]benzenesulfonamide as a white solid in 48% yield. MS (ESI) 827.2 (M+H)

EXAMPLE 133

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide

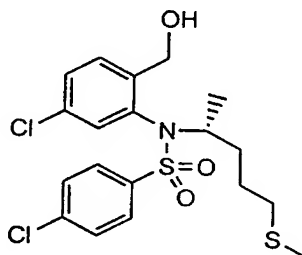


To a solution of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]-benzenesulfonamide (0.650 g, 1.24 mmol) in tetrahydrofuran (2 mL) was added sodium thioethoxide (0.115 g, 1.36 mmol) under nitrogen at 0 °C. The mixture was stirred overnight at 22 °C.

The mixture was quenched with 2M NaOH (3 mL), extracted with ethyl ether (2 x 20 mL), dried over Na₂SO₄, and filtered. The organic solvent was concentrated under reduced pressure. Silica gel chromatography (1:9 ethyl acetate:hexanes) afforded 0.500 g of 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide as a yellow oil in 87% yield. MS (ESI+), 462(M+H)+.

EXAMPLE 134

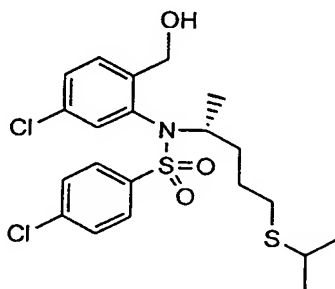
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylthio)butyl]benzenesulfonamide



4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(methylthio)]-1-(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with sodium thiomethoxide. Yield=77%; MS (ESI+), 448(M+H)+.

EXAMPLE 135

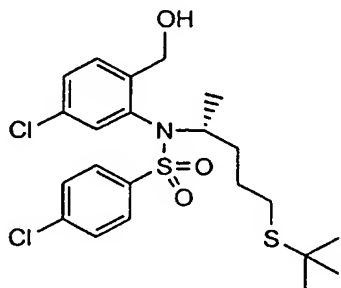
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl]benzenesulfonamide



4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[(1-methylethyl)thio]-1-(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with sodium thio-isopropoxide. Yield=84%; MS (ESI+), 476(M+H)+.

EXAMPLE 136

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)thio]butyl]benzenesulfonamide

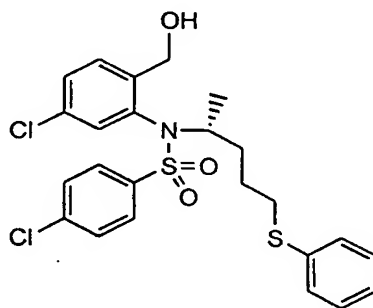


- 5 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)thio]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]-benzenesulfonamide with sodium thio-tert-butoxide. Yield=84%; MS (ESI+), 490(M+H)+.

10

EXAMPLE 137

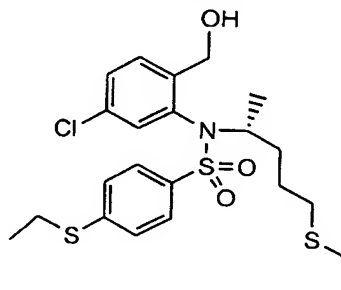
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-phenylthio)butyl]benzenesulfonamide



- 15 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(phenylthio)]-1-(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]-benzenesulfonamide with sodium thiophenoxide. Yield=79%; MS (ESI+), 510(M+H)+.

EXAMPLE 138

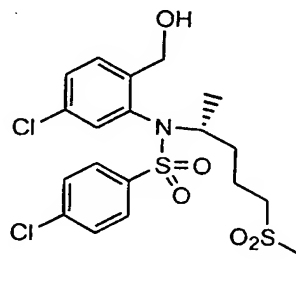
4-ethylthio-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-ethylthio)butyl]benzenesulfonamide



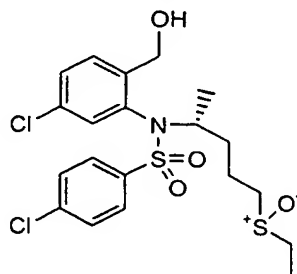
5 To a solution of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide (1.00 g, 1.91 mmol) in DMF (4 mL) was added sodium thioethoxide (0.535 g, 7.63 mmol) under nitrogen at 0 °C. The mixture was stirred overnight at 22 °C. The mixture was quenched with H₂O (3 mL), extracted with ethyl ether (2 x 20 mL), dried over Na₂SO₄, and filtered. The organic solvent was concentrated under reduced pressure. Silica gel chromatography (1:9
10 ethyl acetate:hexanes) afforded 0.123 g of 4-ethylthio-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide as a yellow oil in 14% yield. MS (ESI+), 488 (M+H)+.

EXAMPLE 139

15 **4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[ethylsulfonyl]-1-(R)-methylbutyl]benzenesulfonamide**



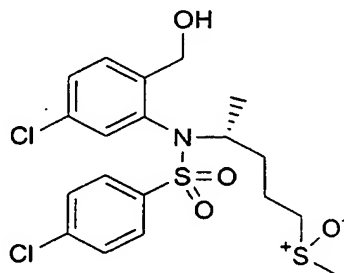
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylsulfinyl)-1-(R)-methylbutyl]benzenesulfonamide



To a solution of 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide (0.088 g, 0.190 mmol) in CH₂Cl₂ (2 mL) was added 80% 3-chloroperoxybezoic acid (0.062 g, 0.285 mmol) at 0 °C. Stirring was continued for 2 h at 22 °C. The mixture was quenched with H₂O (10 mL), extracted with CH₂Cl₂ (2 x 20 mL), dried over Na₂SO₄, and filtered. Solvent was concentrated under reduced pressure to afford a yellow oil. Silica gel chromatography (2% methanol:CH₂Cl₂, 5% methanol:CH₂Cl₂) gave 48.7 mg of 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(ethyl)sulfonyl]-1-(R)-methylbutyl] benzenesulfonamide in 52% yield and 39.8mg of 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[ethyl)sulfinyl]-1-(R)-methylbutyl]benzenesulfonamide in 44% yield; MS (ESI) 494 (M+1); MS (ESI) 478 (M+1).

EXAMPLE 140

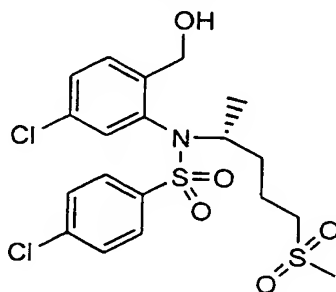
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl]benzenesulfonamide



4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethyl)sulfinyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(methylthio)]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=61%; MS (ESI+), 464(M+H)+.

EXAMPLE 141

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl]benzenesulfonamide

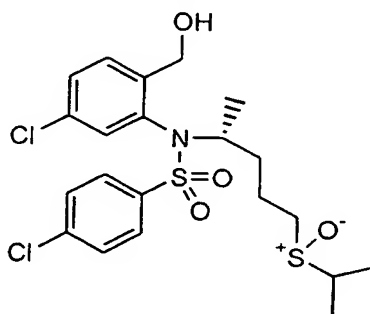


- 5 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[ethylsulfonyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[(methylthio)-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=71%; MS (ESI+), 480(M+H)+.

10

EXAMPLE 142

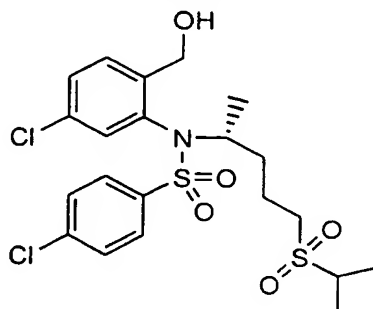
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfinyl]butyl]benzenesulfonamide



- 15 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[(1-methylethyl)sulfinyl]-1-(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethylsulfinyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[(1-methylethyl)thio]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=43%; MS (ESI+), 492(M+H)+.

EXAMPLE 143

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfonyl]butyl]benzenesulfonamide

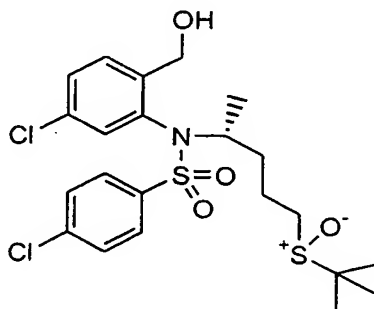


- 5 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[(1-methylethyl)sulfinyl]-1-(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethyl)sulfonyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[(1-methylethyl)thio]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=46%; MS (ESI+), 508(M+H)+.

10

EXAMPLE 144

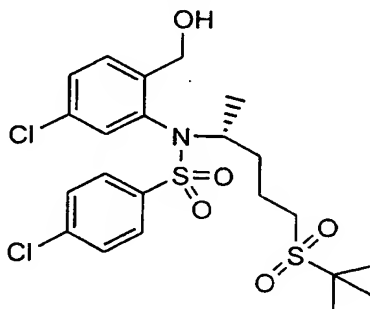
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)sulfinyl]butyl]benzenesulfonamide



- 15 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)sulfinyl]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethyl)sulfinyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)thio]butyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=50%; MS (ESI+), 506(M+H)+.

EXAMPLE 145

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)sulfonyl]butyl]benzenesulfonamide

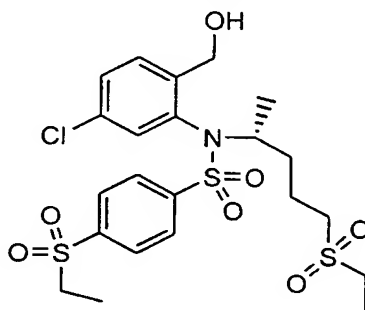


5 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)sulfonyl]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(ethyl)sulfonyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)thio]butyl]-benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=41%; MS (ESI) 522 (M+1).

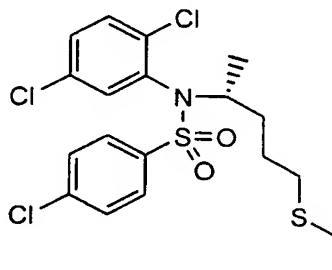
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EXAMPLE 146

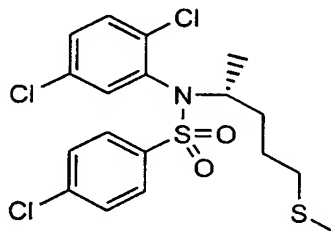
4-ethylsulfonyl-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl]benzenesulfonamide



To a solution of 4-ethylthio-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-ethylthio)butyl]benzenesulfonamide (0.123 g, 0.267 mmol) in CH₂Cl₂ (3 mL) was added 80% 3-chloroperoxybezoic acid (0.231 g, 1.07 mmol) at 0 °C. Stirring was continued for 2h at 22 °C. The mixture was quenched with H₂O (10 mL), extracted with CH₂Cl₂ (2 x 20 mL), dried over Na₂SO₄, and filtered. Solvent was concentrated under reduced pressure to afford a yellow oil. Silica gel chromatography (2% methanol:CH₂Cl₂, 5% methanol:CH₂Cl₂) gave 99.3 mg of 4-ethylsulfonyl-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl]benzenesulfonamide in 71% yield. MS (ESI+), 569(M+NH₃)⁺.

EXAMPLE 147**4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylthio)]-1(R)-methylbutyl] benzenesulfonamide**

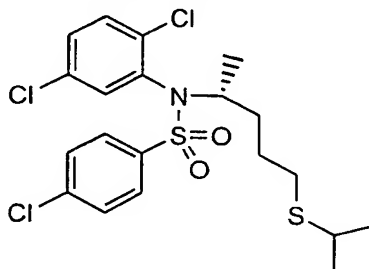
To a solution of NaH (0.025g, 1.03 mmol) in tetrahydrofuran (2 mL) was added ethanethiol
5 (0.096 g, 1.54 mmol), followed by 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide (0.500 g 1.03 mmol) under nitrogen at 0°C. The reaction was stirred overnight at 22 °C. The mixture was quenched with H₂O (3 mL), extracted with ethyl ether (2 x 10 mL), dried over Na₂SO₄, and filtered. The organic solvent was concentrated under reduced pressure.
10 Silica gel chromatography (1:9, ethyl acetate:hexanes) afforded 0.460g of 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylthio)]-1(R)-methylbutyl]benzenesulfonamide as a yellow oil in 59% yield. LC/MS 466.

EXAMPLE 148**4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylthio)butyl]benzenesulfonamide**

15 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylthio)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-ethylthio)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with sodium thiomethoxide. Yield=100%; MS (ESI+), 452(M+H)+.

EXAMPLE 149

4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl]benzenesulfonamide

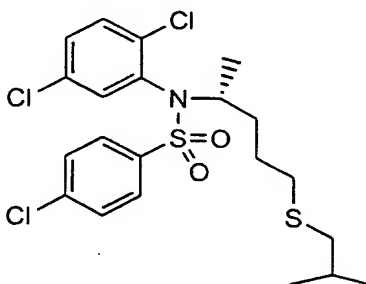


5 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-ethylthio)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with sodium thio-iso-propoxide. Yield=100%; MS (ESI+), 478(M-H)+.

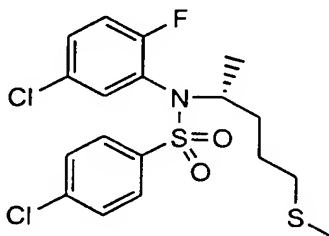
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EXAMPLE 150

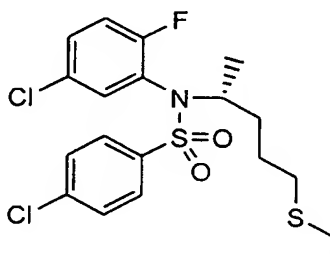
4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)thio)sulfonyl]butyl]benzenesulfonamide



15 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)thio)sulfonyl]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-ethylthio)butyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with sodium thio-iso-butoxide. Yield=100%; MS (ESI+), 494(M+H)+.

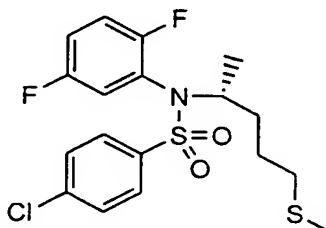
EXAMPLE 151**4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-methylthio)butyl]benzenesulfonamide**

5 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[4-(methylthio)]-1-(R)-methylbutyl]benzene-sulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with sodium thiomethoxide. Yield=98%; MS (ESI+), 436(M+H)⁺.

EXAMPLE 152**4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-ethylthio)butyl]benzenesulfonamide**

10

15 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzene-sulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with sodium thioethoxide. Yield=92%; MS (ESI+), 450(M+H)⁺.

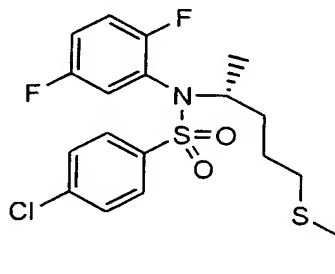
EXAMPLE 153**4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-methylthio)butyl]benzenesulfonamide**

4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-methylthio)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylthio)-1-(R)-methylbutyl]-benzenesulfonamide by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]-benzenesulfonamide with sodium thiomethoxide. Yield= 97%; MS (ESI+), 420 (M+H)+.

5

EXAMPLE 154

4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-ethylthio)butyl]benzenesulfonamide

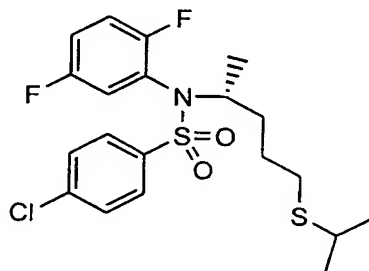


10 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-ethylthio)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylthio)-1-(R)-methylbutyl]-benzenesulfonamide by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-bromo)butyl]-benzenesulfonamide with sodium thioethoxide. Yield= 96%; MS (ESI+), 434(M+H)+.

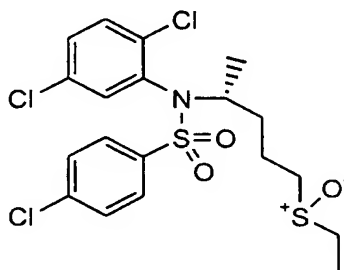
EXAMPLE 155

4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl]benzenesulfonamide

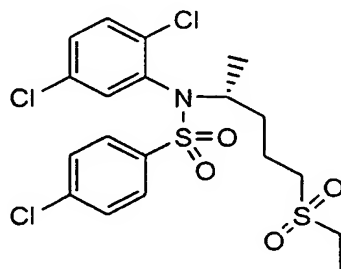
15



20 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylthio)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[(R)-1-methyl-4-bromobutyl]benzenesulfonamide with sodium thio-iso-propoxide. Yield= 89%; MS (ESI+), 448(M+H)+.

EXAMPLE 156**4-chloro-N-[2, 5-dichlorophenyl]-N-[4-(ethylsulfonyl)-1-(R)-methylbutyl]benzenesulfonamide**

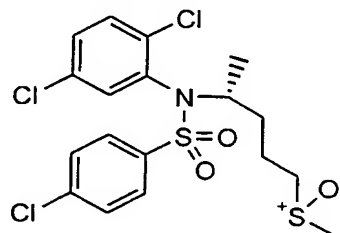
5 **4-chloro-N-[2, 5-dichlorophenyl]-N-[4-(ethylsulfonyl)-1-(R)-methylbutyl] benzenesulfonamide**



To a solution of 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide (0.460 g, 0.600 mmol) in CH₂Cl₂ (6 mL) was added 80% 3-chloroperoxybezoic acid (0.166 g, 0.957 mmol) at 0 °C. Stirring was continued for 2 h at 22 °C. The mixture was quenched with H₂O (10 mL) extracted with CH₂Cl₂ (2 x 10 mL), dried over Na₂SO₄, and filtered. Solvent was concentrated under reduced pressure to afford a yellow oil. Silica gel chromatography (2% methanol:CH₂Cl₂, 5% methanol:CH₂Cl₂) gave 0.170 g of 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(ethyl)sulfonyl]-1-(R)-methylbutyl] benzenesulfonamide in 56% yield and 0.130 g of 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[ethyl sulfoxyl]-1-(R)-methylbutyl] benzene sulfonamide in 44% yield. MS (ESI) 498 (M+1); MS (ESI) 482 (M+1).

EXAMPLE 157

4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl]benzenesulfonamide

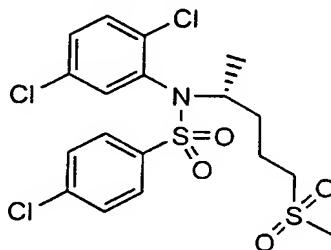


5 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfinyl)]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(methylthio)]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=47%; MS (ESI+), 466(M-H)+.

10

EXAMPLE 158

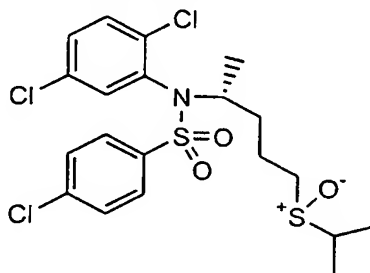
4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl]benzenesulfonamide



15 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfonyl)]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(methylthio)]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=42%; MS (ESI+), 482(M-H)+.

EXAMPLE 159

4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfinyl]butyl]benzenesulfonamide

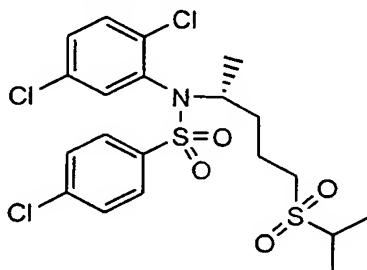


5 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfinyl]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[ethylsulfinyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=54%; MS (ESI+), 496(M+H)+.

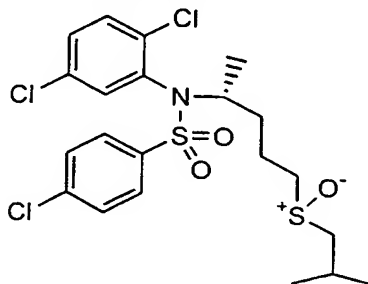
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EXAMPLE 160

4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfonyl]butyl]benzenesulfonamide

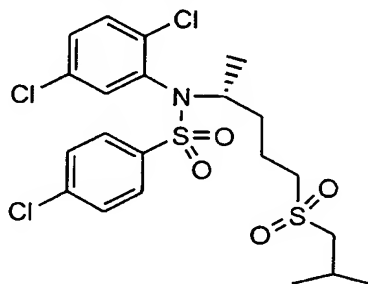


15 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfonyl]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[ethylsulfonyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=38%; MS (ESI+), 512(M+H)+.

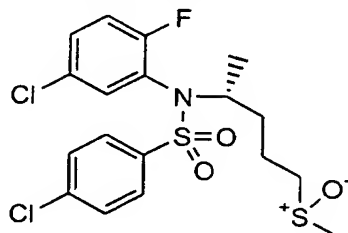
EXAMPLE 161**4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)sulfinyl]butyl)]benzenesulfonamide**

- 5 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)sulfinyl]butyl)]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethyl)sulfinyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)thio]butyl)]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=29%; MS (ESI+), 508(M-H)+.

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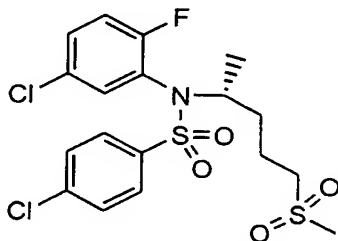
EXAMPLE 162**4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)sulfonyl]butyl)]benzenesulfonamide**

- 15 This compound was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethyl)sulfonyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)thio]butyl)]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=35%; MS (ESI+), 526(M+H)+.

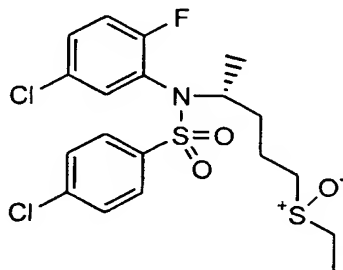
EXAMPLE 163**4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl]benzenesulfonamide**

5 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfinyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[4-(methylthio)-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybenzoic acid. Yield=61%; MS (ESI+), 452(M+H)+.

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EXAMPLE 164**4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl]benzenesulfonamide**

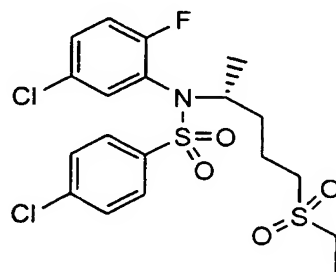
15 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfonyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[4-(methylthio)-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybenzoic acid. Yield=37%; MS (ESI+), 466(M-H)+.

EXAMPLE 165**4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-ethylsulfinyl)butyl]benzenesulfonamide**

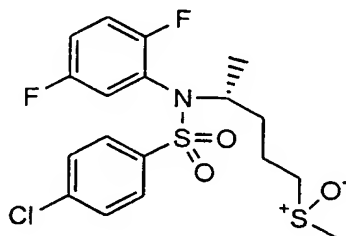
- 5 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-ethylsulfinyl)butyl]benzene-sulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfinyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=48%; MS (ESI+), 466(M+H)+.

EXAMPLE 166

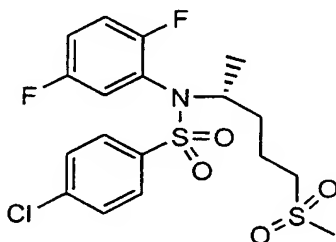
- 10 **4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl]benzenesulfonamide**



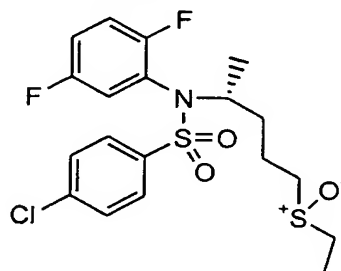
- 15 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl]benzene-sulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfonyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[4-(ethylthio)]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=44%; MS (ESI+), 482(M+H)+.

EXAMPLE 167**4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl]benzenesulfonamide**

4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfinyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[4-(methylthio)]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=35%; MS (ESI+), 436(M+H)+.

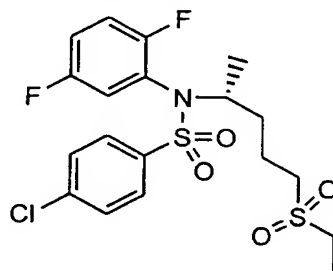
EXAMPLE 168**4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl]benzenesulfonamide**

4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfonyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[4-(methylthio)]-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=30%; MS (ESI+), 452(M+H)+.

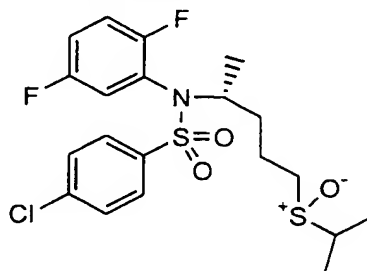
EXAMPLE 169**4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-ethylsulfinyl)butyl]benzenesulfonamide**

5 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-ethylsulfinyl)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfinyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[4-(ethylthio)-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybenzoic acid. Yield=40%; MS (ESI+), 450(M+H)+.

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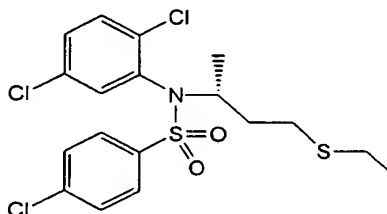
EXAMPLE 170**4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl]benzenesulfonamide**

15 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylsulfonyl)-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[4-(ethylthio)-1-(R)-methylbutyl]benzenesulfonamide with 3-chloroperoxybenzoic acid. Yield=57%; MS (ESI+), 466(M+H)+.

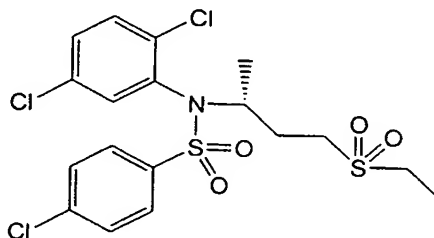
EXAMPLE 171**4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfinyl]butyl]benzenesulfonamide**

5 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfinyl]butyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethyl)sulfinyl]-1-(R)-methylbutyl]benzenesulfonamide by reacting 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl]benzenesulfonamide with 3-chloroperoxybezoic acid. Yield=32%; MS (ESI+), 464(M+H)+.

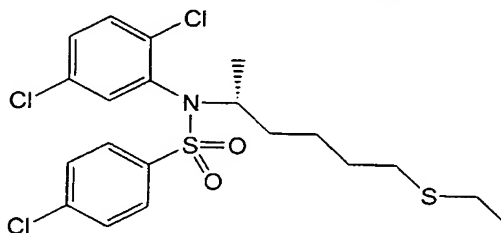
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EXAMPLE 172**4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(3-ethylthio)propyl] benzenesulfonamide**

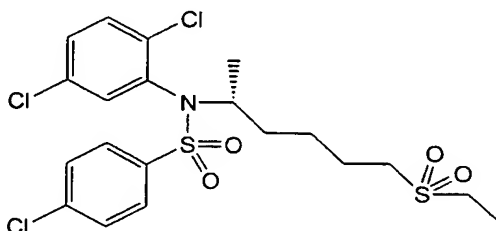
To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[1(R)-methyl-(3-iodo)propyl]benzenesulfonamide (0.500 g, 0.960 mmol) in THF (2 mL) was added sodium thioethoxide (0.080 g, 0.960 mmol) at 22 °C. The reaction was allowed to stir for 12 h at 22 °C. The solvent was removed, the residue was taken into CH₂Cl₂ (50 mL) and washed with water (50 mL). The organic solution was dried over Na₂SO₄, filtered and concentrated to afford (0.330 g) of 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(3-ethylthio)propyl] benzenesulfonamide as a colorless oil in 77% yield. MS (ESI+), (M+H)+.

EXAMPLE 173**4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(3-ethylsulfonyl)propyl] benzenesulfonamide**

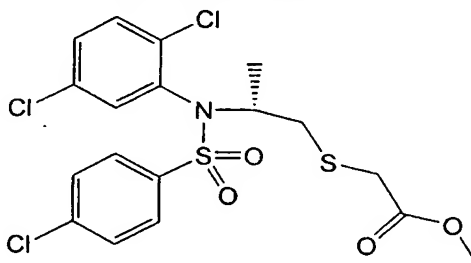
To a solution of 4-chloro-N-[2,5-dichlorophenyl]-N-[(R)-1-methyl-(3-ethylthio)propyl]benzenesulfonamide (0.330 g, 0.730 mmol) was added 3-chloroperoxybenzoic acid, (0.250 g, 0.960 mmol) in THF (1 mL) at 22 °C. After 2 h the mixture was washed with water (50 mL) and extracted with ether (50 mL). The organic solution was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Silica gel chromatography (5% CH₂Cl₂/methanol) of the concentrate gave 0.198 g of 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(3-ethylsulfonyl)propyl] benzenesulfonamide in 56% yield. MS ESI (483).

EXAMPLE 174**4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(5-ethylthio)pentyl] benzenesulfonamide**

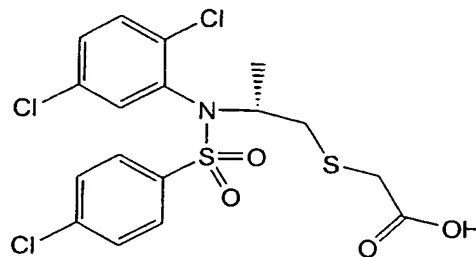
To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[1(R)-methyl-(5-iodo)pentyl] benzenesulfonamide (0.500 g, 0.938 mmol) in THF (8 mL) was added sodium thioethoxide (0.078 g, 9.38 mmol) at 22 °C. After 12 h the solvent was removed, the residue was taken into CH₂Cl₂ (50 mL) and washed with water. The organic solution was dried over Na₂SO₄, filtered and concentrated to afford (0.300 g) of 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(5-ethylthio)pentyl] benzenesulfonamide as a colorless oil in 67% yield.

EXAMPLE 175**4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(5-ethylsulfonyl) pentyl]benzenesulfonamide**

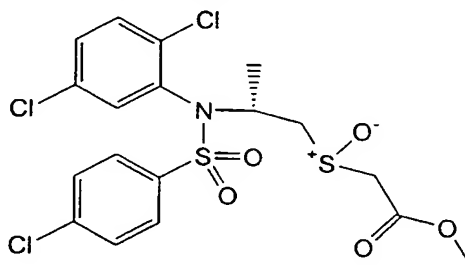
5 To a solution of 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(5-ethylthio)pentyl]benzenesulfonamide (0.300 g, 0.650 mmol) was added 3-chloroperoxybenzoic acid, (0.170 g, 0.970 mmol) in CH₂Cl₂ (1.5 mL). Stirring was continued for 2 h at 22 °C. The product was washed with water (50 mL) and extracted with CH₂Cl₂ (50 mL). The organic solution was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Silica gel chromatography (5% CH₂Cl₂/methanol) of the concentrate gave 0.062 g of 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(5-ethylsulfonyl) pentyl]benzenesulfonamide in 19% yield. MS ESI (511).

EXAMPLE 176**methyl(5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thiohexanoate**

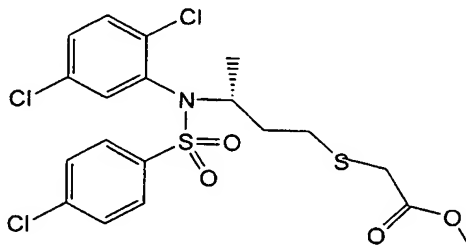
15 To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[(R)-1-methyl(2-iodoethyl)]benzenesulfonamide (0.840 g, 1.66 mmol) and methyl thioglycolate (1.05 g, 9.90 mmol) in diethyl ether was added triethylamine (1.33 g, 13.2 mmol) at 22 °C. This mixture was heated to reflux for 12h. The product was washed with aqueous NaHCO₃, extracted with diethyl ether, dried over Na₂SO₄ and filtered. Concentration in vacuo, followed by silica gel chromatography (15% ethyl acetate/hexanes) of the concentrate produced the title compound (800 mg, 98% yield).

EXAMPLE 177**methyl(5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thiohexanoic acid**

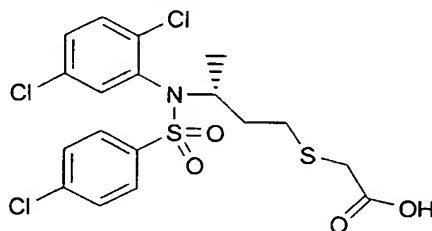
To a solution of methyl(5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl) sulfonyl]amino]-3-thiohexanoate (0.050 g, .1.00 mmol) in methanol (1 mL) was added 1 mL of 0.5M sodium hydroxide at 22 °C. The mixture was stirred for 1h. The methanol was evaporated. The residue was diluted with ether and washed with water. The collected aqueous layer was acidified with 1N hydrochloride, and extracted with ether (2 x 50 mL). The organic layer was dried over Na₂SO₄, filtered and concentrated under reduced pressure to afford methyl(5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thiohexanoate (33.3 mg, 70% yield). MS ESI (467).

EXAMPLE 178**methyl(5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thiohexanoate,3 oxide**

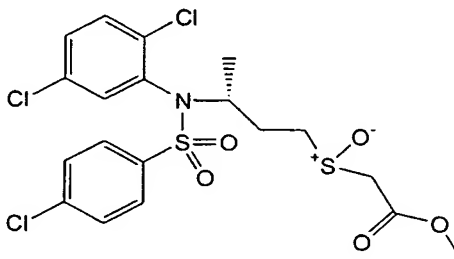
To a solution of methyl(5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl) sulfonyl]amino]-3-thiohexanoate (0.790 g, 1.70 mmol) in CH₂Cl₂ (2 mL) was added 3-chloroperoxybenzoic acid (0.350g, 2.00 mmol) at 22 °C. The mixture was allowed to stirred for 2h. The mixture was diluted with CH₂Cl₂, washed with water, dried over Na₂SO₄ and filtered. Silica gel chromatography (10% CH₂Cl₂/methanol) afforded methyl(5R)-5-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thiohexanoate,3 oxide (0.380 g, 46% yield). MS ESI (497).

EXAMPLE 179**methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoate**

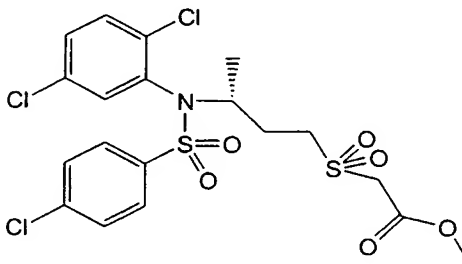
To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[1(R)-methyl-(3-iodo)-propyl] benzenesulfonamide (0.850 g, 1.64 mmol) and methyl thioglycolate (0.174 g, 1.60 mmol) in diethyl ether was added triethylamine (1.94 g, 1.92 mmol) at 22 °C. This mixture was heated to reflux for 12h. The product was washed with aqueous NaHCO₃, extracted with diethyl ether, dried over Na₂SO₄ and filtered. Concentration under reduced pressure, followed by silica gel chromatography (15% ethyl acetate/hexane) of the concentrate produced methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoate (0.650 g, 80% yield). MS ESI (495).

EXAMPLE 180**(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoic acid**

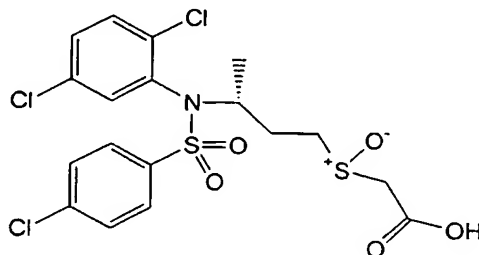
To a solution of methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoate (0.100 g, 0.200 mmol) 2 mL of methanol was added 1M sodium hydroxide (1 mL) at 22 °C. The mixture was stirred for 1h and the methanol was evaporated. The residue was diluted with ether and washed with water. The collected aqueous layer was acidified with 1N hydrochloride, and extracted with ether (3 x 25mL). The organic layer was dried over Na₂SO₄, filtered and concentrated under reduced pressure to afford (6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoic acid (0.090 g, 90% yield). MS ESI (481).

EXAMPLE 181**methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoate, 3-oxide**

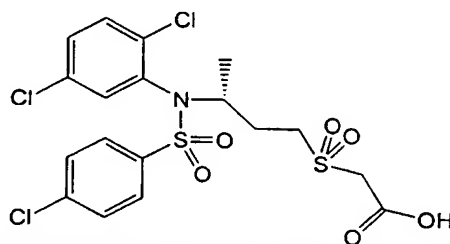
5 **methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoate, 3,3
dioxide**



To a solution of methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl) sulfonyl]amino]-3-thioheptanoate (0.650 g, 1.30 mmol) in CH₂Cl₂ (5 mL) was added 3-chloro-peroxybenzoic acid (0.452 g, 2.60 mmol) at 22 °C. The mixture was allowed to stir for 2h. The solution was washed with water,
10 extracted with CH₂Cl₂, dried over Na₂SO₄ and filtered. Silica gel chromatography (10% CH₂Cl₂/methanol) of the concentrate afforded (0.380g) of methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoate, 3-oxide in 46% yield and (0.340 g) of methyl(6R)-6-[(2,5-dichlorophenyl) [(4-chlorophenyl) sulfonyl] amino]-3-thio heptanoate, 3,3 dioxide in 50% yield.
15 MS ESI (511). MS ESI (527).

EXAMPLE 182**(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoic acid, 3-oxide**

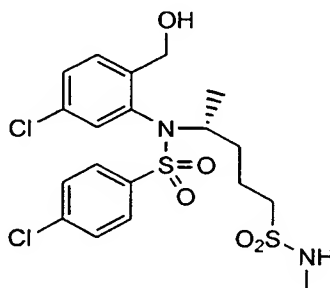
5 To a solution of methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoate, 3-oxide (0.150 g, 0.290 mmol) in 4 mL of methanol was added 1M sodium hydroxide (2 mL) at 22 °C. The mixture was stirred for 1h and the methanol was evaporated. The residue was diluted with ether and washed with water. The collected aqueous layer was acidified with 1N hydrochloride, and extracted with ether (3 x 50 mL). The organic layer was dried over Na₂SO₄, filtered
 10 and concentrated under reduced pressure to afford (6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoic acid, 3-oxide (0.130 g, 85% yield). MS ESI (497).

EXAMPLE 183**(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoic acid, 3,3 dioxide**

15 To a solution of methyl(6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoate, 3,3dioxide (0.150 g, 2.90 mmol) in 4 mL of methanol was added 1M sodium hydroxide (2 mL) at 22 °C. The mixture was stirred for 1h and the methanol was evaporated. The residue was diluted with ether and washed with water. The collected aqueous layer was acidified with 1N hydrochloride, and extracted with ether (3 x 50 mL). The organic layer was dried over Na₂SO₄, filtered
 20 and concentrated under reduced pressure to afford (6R)-6-[(2,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amino]-3-thioheptanoic acid, 3,3 dioxide (0.140 g, 90% yield). MS ESI (513).

EXAMPLE 184

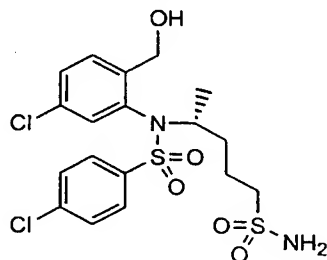
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide



5 To a solution of (4R)-4-[5-chloro-2-(acetoxymethyl)phenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride (150 mg, 0.276 mmol) in CH_2Cl_2 (2 ml) was added a 2M THF solution of methylamine (1.38 mL, 2.76 mmol). The mixture was stirred at 22 °C overnight. 1N HCl (1 mL) was added to the mixture, followed by extraction with CH_2Cl_2 . The organic layer was dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to afford a colorless oil. This oil was
10 purified by prep HPLC to afford 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide in 64% yield. MS (ESI) 495 (M+1).

EXAMPLE 185

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(aminosulfonyl)-1(R)-methylbutyl]benzenesulfonamide



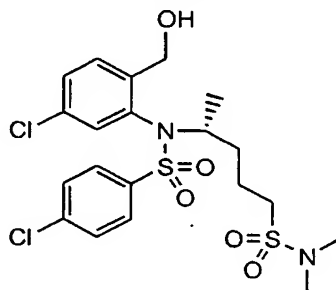
15

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(aminosulfonyl)-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[5-chloro-2-(acetoxymethyl)phenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with ammonia.

20 Yield=60%.; MS (ESI+), 481(M+H)⁺.

EXAMPLE 186

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(dimethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

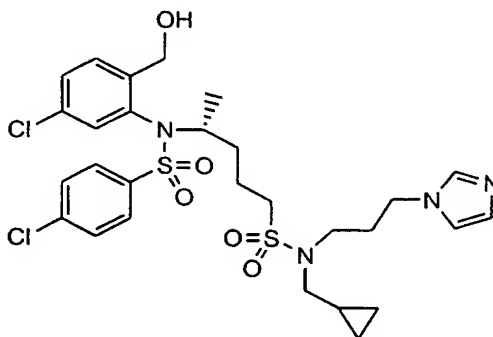


5 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(dimethylaminoaminosulfonyl)-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[5-chloro-2-(acetoxymethyl)phenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with dimethylamine. Yield=73%; MS (ESI+), 509(M+H)+.

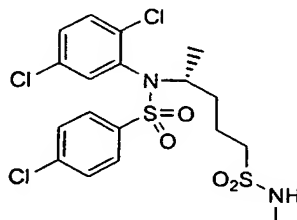
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EXAMPLE 187

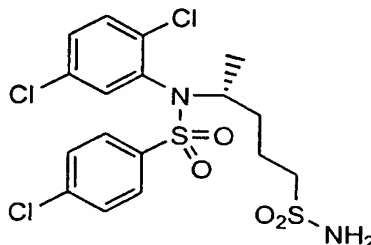
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[N-(cyclopropylmethyl)-N-[3-(1H-imidazol-1-yl)propyl]aminosulfonyl]-1(R)-methylbutyl]benzenesulfonamide



15 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[N-(cyclopropylmethyl)-N-[3-(1H-imidazol-1-yl)propyl]aminosulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[5-chloro-2-(acetoxymethyl)phenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with N-(cyclopropylmethyl)-N-[3-(1H-imidazol-1-yl)propyl]amine. Yield=49%; MS (ESI+), 643(M+H)+.

EXAMPLE 188**4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide**

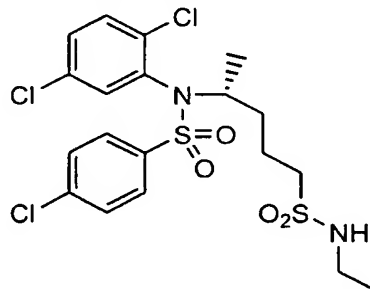
To a solution of (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl] sulfonyl-amino] pentylsulfonyl chloride (212 mg, 1.69 mmol) in CH_2Cl_2 (2 ml) was added methylamine (52.0 mg, 6.76 mmol). The mixture was stirred at 22 °C overnight. 1N HCl (1 mL) was added to the mixture, followed by extraction with CH_2Cl_2 . The organic layer was dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to afford a colorless oil. This oil was purified by prep HPLC to afford 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide in 84% yield. MS (ESI) 499 (M+1).

EXAMPLE 189**4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(amino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide**

4-chloro-N-[2,5-dichlorophenyl]-N-[4-(aminosulfonyl)-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl]sulfonyl-amino]pentylsulfonyl chloride with ammonia. Yield=41%; MS (ESI+), 485(M+H)+.

EXAMPLE 190

4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(ethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

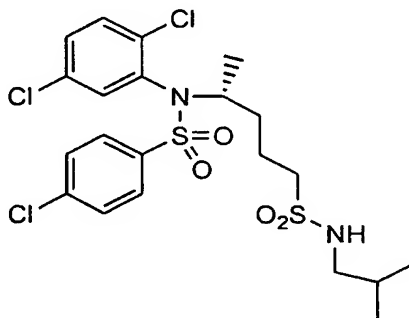


- 5 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(ethylaminosulfonyl)-1(R)-methylbutyl]benzene-sulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with ethylamine. Yield=37%; MS (ESI+), 513(M+H)+.

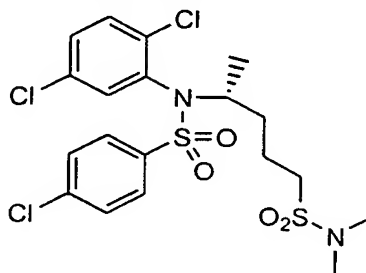
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EXAMPLE 191

4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(2-methylpropylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

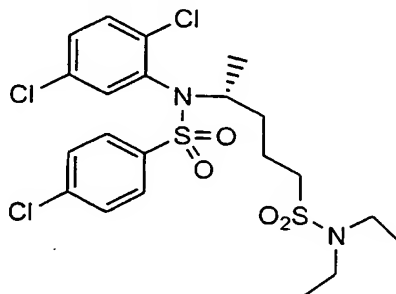


- 15 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(2-methylpropylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with iso-butylamine. Yield=66%; MS (ESI+), 541(M+H)+.

EXAMPLE 192**4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(dimethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide**

- 5 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(dimethylaminosulfonyl)-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with dimethylamine. Yield=65%; MS (ESI+), 513(M+H)+.

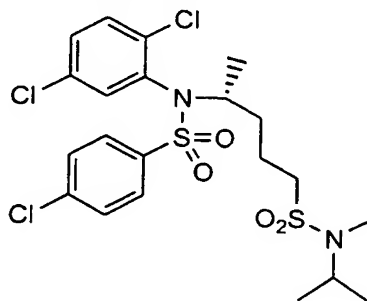
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EXAMPLE 193**4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(diethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide**

- 15 4-chloro-N-[2,5-dichlorophenyl]-N-[4-(diethylaminosulfonyl)-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with diethylamine. Yield=59%; MS (ESI+), 541(M+H)+.

EXAMPLE 194

4-chloro-N-[2,5-dichlorophenyl]-N-[4-[[N-(1-methylethyl)methylamino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

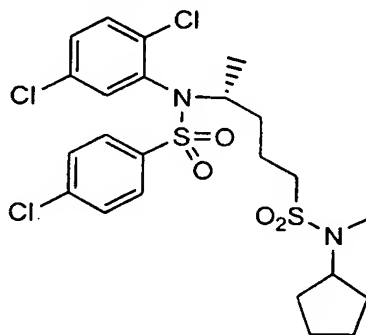


5 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[[N-(1-methylethyl)methylamino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with N-(1-methylethyl)-methylamine. Yield=37%; MS (ESI+), 541(M+H)⁺.

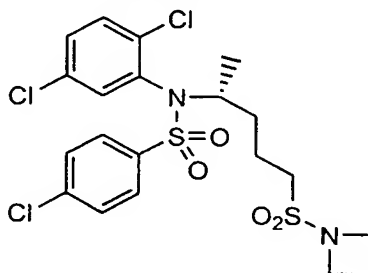
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EXAMPLE 195

4-chloro-N-[2,5-dichlorophenyl]-N-[4-[[N-(cyclopentyl)methylamino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

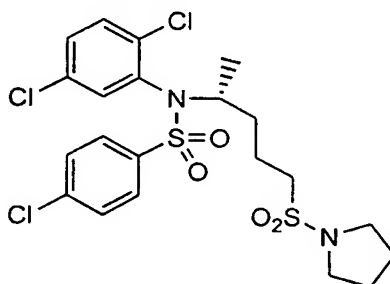


15 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[[N-(cyclopentyl)methylamino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with N-(cyclopentyl)-methylamine. Yield=15%; MS (ESI+), 567(M+H)⁺.

EXAMPLE 196**4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(1-azetidiny)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide**

- 5 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(1-azetidiny)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with azetidine. Yield=24%; MS (ESI+), 526(M+H)+.

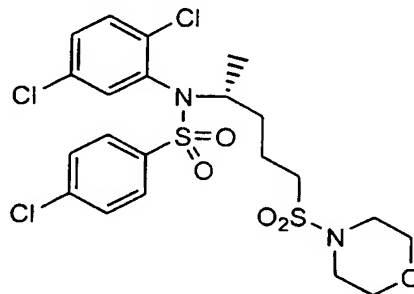
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EXAMPLE 197**4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(1-pyrrolidiny)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide**

- 15 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(1-pyrrolidiny)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with pyrrolidine. Yield=61%; MS (ESI+), 539(M+H)+.

EXAMPLE 198

4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(4-morpholinyl)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

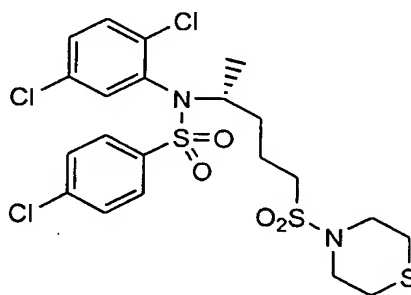


5 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(1-morpholinyl)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with morpholine. Yield=37%; MS (ESI+), 555(M+H)+.

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EXAMPLE 199

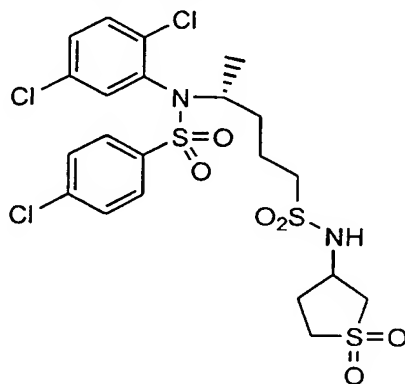
4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(4-thiomorpholinyl)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide



15 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(4-thiomorpholinyl)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with thiomorpholine. Yield=64%; MS (ESI+), 571(M+H)+.

EXAMPLE 200

4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(tetrahydro-1,1-dioxido-3-thienyl)amino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

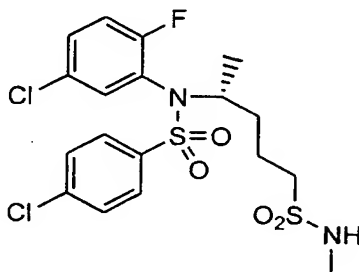


- 5 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(tetrahydro-1,1-dioxido-3-thienyl)amino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-dichlorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with tetrahydro-1,1-dioxido-3-thienylamine. Yield=23%; MS (ESI+), 603(M+H)+.

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EXAMPLE 201

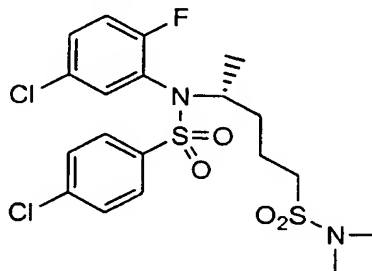
4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide



- 15 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[4-(methylaminosulfonyl)-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[5-chloro-2-fluorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with methylamine. Yield=81%; MS (ESI+), 483(M+H)+.

EXAMPLE 202

4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(dimethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

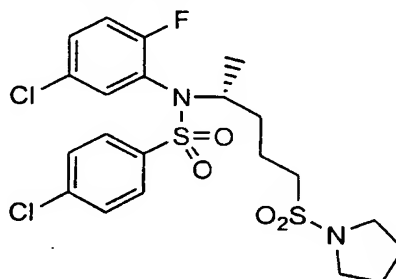


5 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[4-(dimethylaminosulfonyl)-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[5-chloro-2-fluorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with dimethylamine. Yield=85%; MS (ESI+), 497(M+H)+.

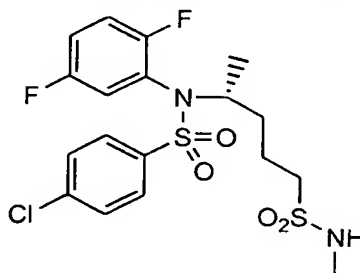
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EXAMPLE 203

4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(1-pyrrolidiny)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide

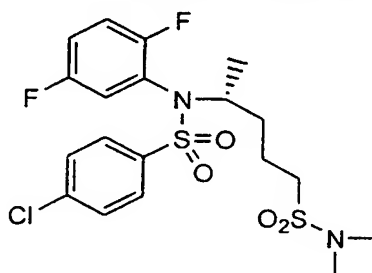


15 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(1-pyrrolidiny)sulfonyl]-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[5-chloro-2-fluorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with pyrrolidine. Yield=86%; MS (ESI+), 523(M+H)+.

EXAMPLE 204**4-chloro-N-[2,5-difluorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide**

5 4-chloro-N-[2,5-difluorophenyl]-N-[4-(methylaminosulfonyl)-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-difluorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with methylamine. Yield=86%; MS (ESI+), 467(M+H)+.

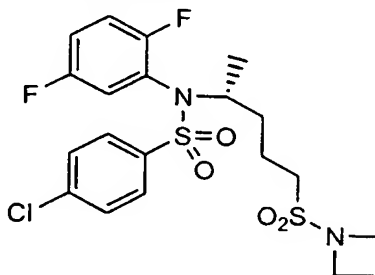
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EXAMPLE 205**4-chloro-N-[2,5-difluorophenyl]-N-[4-[(dimethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide**

15 4-chloro-N-[2,5-difluorophenyl]-N-[4-(dimethylaminosulfonyl)-1(R)-methylbutyl]-benzenesulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-difluorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with dimethylamine. Yield=90%; MS (ESI+), 481 (M+H)+.

EXAMPLE 206

4-chloro-N-[2,5-difluorophenyl]-N-[4-[(1-azetidiny)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide



5 4-chloro-N-[2,5-difluorophenyl]-N-[4-[(1-azetidiny)sulfonyl]-1(R)-methylbutyl]benzene-sulfonamide was prepared analogous to 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl] benzenesulfonamide by reacting (4R)-4-[2,5-difluorophenyl][4-chlorophenyl)sulfonyl]-amino]pentylsulfonyl chloride with azetidine. Yield=50%; MS (ESI+), 493(M+H)+.

10

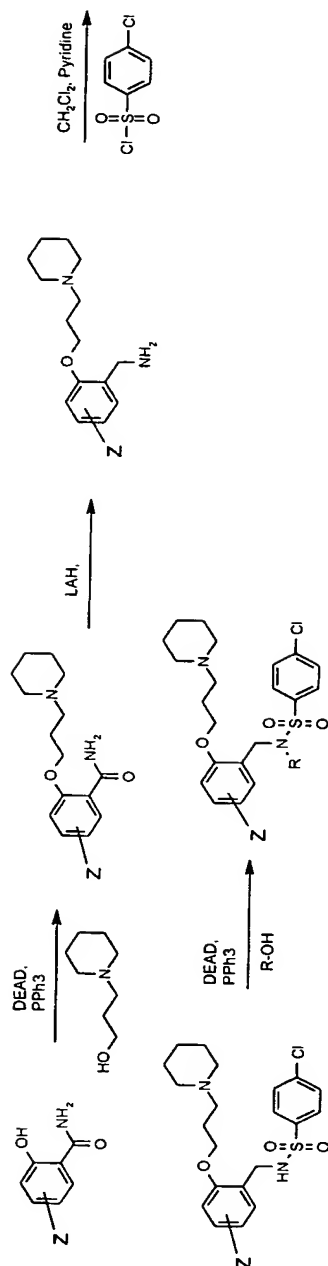
EXAMPLE 207

The general reaction scheme outlined in **Scheme 207** is described in detail in the text following the scheme.

15

120

SCHEME 207



To a stirred solution of salicylamide (1.5 g, 11 mmol) in benzene (15 mL) at room temperature (room temperature) was added *N*-(3-hydroxypropyl)piperidine (1.43 g, 10 mmol), triphenylphosphine (Triphenylphosphine) (2.62 g, 10 mmol) followed by diethylazodicarboxylate (DEAD), (1.74g, 10.0 mmol) in benzene (5 mL) over a period of 15 min. The reaction mixture was then left stirred at room temperature for 40 h, concentrated under reduced pressure. The residue was re-dissolved in methylene chloride (DCM; 100 mL). The DCM solution was washed with 1.0 N NaOH (2 x 75 mL), water (2 X 75 mL) and extracted with 1.0 N HCl (3 x 40 mL). The HCl solution was basified with solid NaOH to pH 14 to yield a turbid solution that was extracted with DCM (2 x 50 mL). The combined DCM solution was washed with water (2 x 50 mL), dried with anhydrous MgSO₄, filtered and concentrated under reduced pressure to yield 2.05 g of pale yellow oil (y: 78%). ¹H NMR (300 MHz, CDCl₃) δ (ppm): 8.20 (dd, 1H), 7.9 (br, 1H), 7.44 (m, 1H), 7.05 (t, 1H), 7.99 (d, 1H), 6.6 (b, 1H), 4.15, (t, 2H), 2.65-2.27 (m, 6H), 2.05 (p, 2H), 1.67-1.54 (m, 2H), 1.45-1.38 (m, 2H).

To a stirred solution of the above amide (1.5 g, 4.6 mmol) in anhydrous THF(40 mL) at room temperature was added solid lithium aluminum hydride (lithium aluminum hydride) (473 mg, 11.8 mmol). The reaction mixture was heated at refluxing conditions for 6 h, cooled to room temperature then quenched with 1.0 N NaOH (0.5 mL). The precipitate was filtered through celite and the celite pad was washed with ethyl acetate (30 mL). The filtrate was diluted with ethyl acetate (100 mL) and washed with water (2 x 75 mL), dried with anhydrous MgSO₄, filtered and concentrated to give 1.1 g of product as colorless oil (y: 96%). ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.26-7.20 (m 2H), 6.90-6.86 (m, 2H), 4.02 (t, 2H), 3.84 (s, 3H), 2.59-2.43 (m, 6H), 2.06 (d, 2H), 1.68-1.56 (m, 4H), 1.48-1.46 (m, 2H).

To a cooled (0 °C, ice bath) solution of the diamine (500 mg, 2.0 mmol) in of DCM (20 mL) was added dry pyridine (164 µL, 2.0 mmol), followed by 4-chlorobenzenesulfonylchloride (422 mg, 2.0 mmol). The reaction mixture was allowed to stir at 0 °C for 2 h then concentrated under reduced pressure. Recrystallization (ethyl acetate/hexanes) of the crude mixture afforded the desired product as HCl salt. (840 mg of pale yellow solid, y: 99%). ¹H NMR (CDCl₃) δ (ppm): (7.64-7.59 (m, 2H), 7.34-7.26, (m, 2H), 7.20, (t, 1H), 7.28-7.24, (m, 1H), 6.86 (m, 1H), 6.61 (d, 1H), 4.10 (t, 2H), 4.04 (d, 2H), 3.54 (d, 2H), 3.43 (t, 2H), 2.76-2.72 (m, 2H), 2.52-2.43 (m, 2H), 2.20-2.00 (m, 2H), 1.87-1.72 (m 4H).

General procedure for the Mitsunobu alkylation of Sulfonamide with alcohols

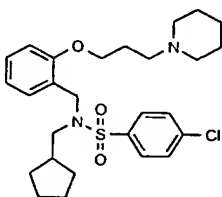
To a solution of the sulfonamide (AA) (1.0 mmol) in anhydrous THF (10 mL) at room temperature was added Triphenylphosphine (1.5 mmol) followed by the appropriate alcohol (1.5 mmol) and DEAD (1.5 mmol) in that order. The clear reaction mixture was stirred at RT for 24 h then concentrated under reduced pressure. The crude product was purified by silica gel chromatography (multiple elution, 200 mL of ethyl acetate, 300-500 mL of 0.5% triethylamine, 0.5% methanol in ethyl

acetate). The desired product was isolated as a colorless oil (45-65% yield). The free base was dissolved in DCM to which an excess of a 1.0 M solution of HCl in ether was added. The resulting solution was concentrated under reduced pressure to give a colorless solid. The HCl salt was purified by passing through a short column of silica (10% methanol in DCM) to afford the desired product in good yield.

The compounds of Examples 208-222 were prepared according to the scheme described in the previous example.

EXAMPLE 208

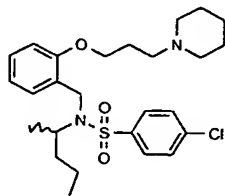
4-chloro-N-(cyclopentylmethyl)-N-{2-[3-(1-piperidinyloxy)benzyl]benzenesulfonamide hydrochloride



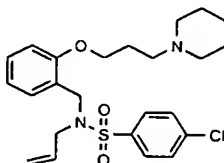
$R_f = 0.34$ (5% methanol, 1% triethylamine in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.82-7.80 (m, 2H), 7.65-7.62 (m, 2H), 7.35 (t, 1H), 7.22-7.17 (m, 1H), 6.95-6.90 (m, 2H), 4.31 (s, 2H), 4.14 (t, 2H), 3.67-3.45 (m, 4H), 3.03 (t, 2H), 2.36 (d, 2H), 2.44-2.35 (m, 2H), 2.03-1.84 (m, 5H), 1.66-1.62 (m, 2H), 1.38-1.24 (m, 6H), 0.97-0.96 (m, 2H).

EXAMPLE 209

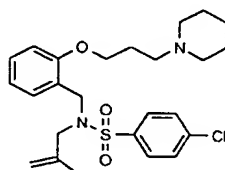
4-chloro-N-(1-methylbutyl)-N-{2-[3-(1-piperidinyloxy)benzyl]benzenesulfonamide hydrochloride



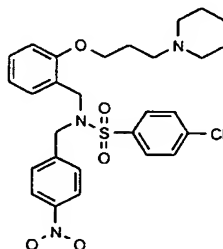
$R_f = 0.34$ (5% methanol, 1% triethylamine in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.84-7.82 (m, 2H), 7.62-7.60 (m, 2H), 7.35-7.26 (m, 2H), 6.97-6.89 (m, 2H), 4.90 (d, 1H), 4.32 (d, 1H), 4.13 (t, 2H), 3.84 (m, 1H), 3.59-3.40 (m, 4H), 3.03-2.96 (m, 2H), 2.36-2.27 (m, 2H), 1.97-1.48 (m, 6H), 1.15-0.97 (m, 4H), 0.83 (d, 3H), 0.63 (t, 3H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm) 159.3, 141.0, 138.0, 132.1, 130.6, 130.5, 129.9, 126.6, 121.8, 112.3, 66.0, 56.1, 55.4, 54.5, 44.2, 38.6, 25.3, 24.3, 22.8, 20.8, 18.2, 14.0. ESI calculated for $\text{C}_{26}\text{H}_{37}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 493; Observed: 493.

EXAMPLE 210**N-allyl-4-chloro-N-{2-[3-(1-piperidinyloxy)propoxy]benzyl}benzenesulfonamide hydrochloride**

$R_f = 0.28$ (1% triethylamine/5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.64 (m, 2H), 7.40 (m, 2H), 7.09 (m, 1H), 6.95 (m, 1H), 6.71 (dt, 2H), 5.14 (m, 1H), 4.65 (d, 2H), 4.22 (s, 2H), 3.90 (t, 2H), 3.46-3.16 (m, 6H), 2.80 (m, 2H), 2.06 (m, 2H), 1.78-1.29 (m, 6H).

EXAMPLE 211**4-chloro-N-(2-methyl-2-propenyl)-N-{2-[3-(1-piperidinyloxy)propoxy]benzyl}benzenesulfonamide hydrochloride**

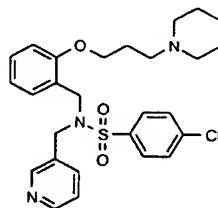
$R_f = 0.26$ (1% triethylamine/5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.62 (m, 2H), 7.41 (m, 2H), 7.08 (m, 1H), 6.91 (dd, 1H), 6.67 (dt, 2H), 4.39 (s, 2H), 4.19 (s, 2H), 3.89 (t, 2H), 3.46-3.27 (m, 6H), 2.82 (m, 2H), 2.09 (m, 2H), 1.81-1.11 (m, 9H).

EXAMPLE 212**4-chloro-N-(4-nitrobenzyl)-N-{2-[3-(1-piperidinyloxy)propoxy]benzyl}benzenesulfonamide hydrochloride**

$R_f = 0.24$ (19:1; DCM:methanol). ^1H NMR (CD_3OD) δ (ppm): 7.86-7.81 (m, 4H), 7.60 (m, 2H), 7.10-6.99 (m, 4H), 6.66 (t, 1H), 6.48 (d, 1H), 4.33 (s, 2H), 4.19 (s, 2H), 3.82 (t, 2H), 3.56-3.45 (m, 4H), 2.98-2.96 (m, 2H), 2.24-2.14 (m, 2H), 1.72-1.36 (m, 6H).

EXAMPLE 213

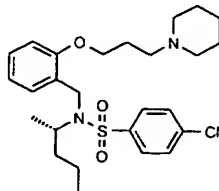
4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}-N-(3-pyridinylmethyl)benzenesulfonamide hydrochloride



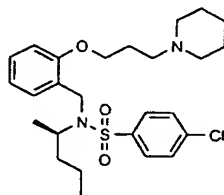
5 $R_f = 0.20$ (4% methanol, 1% triethylamine in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 8.25-8.15 (m, 2H), 7.96-7.93 (m, 2H), 7.71-7.68 (m, 2H), 7.43 (d, 1H), 7.17-7.11 (m, 3H), 6.81-6.79 (m, 1H), 6.60-6.57 (m, 1H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.5, 148.9, 147.6, 140.7, 138.3, 138.1, 133.0, 131.6, 131.0, 130.3, 123.6, 121.8, 111.8, 65.5, 56.1, 54.6, 51.7, 50.3, 25.3, 24.4, 22.9.

EXAMPLE 214

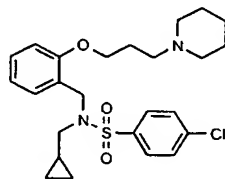
10 **4-chloro-N-[(1R)-1-methylbutyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**



15 $R_f = 0.28$ (4% methanol, 1% triethylamine in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.84-7.82 (m, 2H), 7.62-7.60 (m, 2H), 7.35-7.26 (m, 2H), 6.97-6.89 (m, 2H), 4.90 (d, 1H), 4.32 (d, 1H), 4.13 (t, 2H), 3.84 (m, 1H), 3.59-3.40 (m, 4H), 3.03-2.96 (m, 2H), 2.36-2.27 (m, 2H), 1.97-1.48 (m, 6H), 1.15-0.97 (m, 4H), 0.83 (d, 3H), 0.63 (t, 3H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 159.3, 141.0, 138.0, 132.1, 130.6, 130.5, 129.9, 126.6, 121.8, 112.3, 66.0, 56.1, 55.4, 54.5, 44.2, 38.6, 25.3, 24.3, 22.8, 20.8, 18.2, 14.0. ESI calculated for $\text{C}_{26}\text{H}_{37}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 493; Observed: 493.

EXAMPLE 215**4-chloro-N-[(1S)-1-methylbutyl]-N-{2-[3-(1-piperidinyloxy)benzyl]benzenesulfonamide hydrochloride**

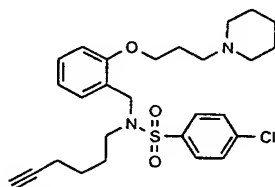
- 5 $R_f = 0.28$ (4% methanol, 1% triethylamine in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.84-7.82 (m, 2H), 7.62-7.60 (m, 2H), 7.35-7.26 (m, 2H), 6.97-6.89 (m, 2H), 4.90 (d, 1H), 4.32 (d, 1H), 4.13 (t, 2H), 3.84 (m, 1H), 3.59-3.40 (m, 4H), 3.03-2.96 (m, 2H), 2.36-2.27 (m, 2H), 1.97-1.48 (m, 6H), 1.15-0.97 (m, 4H), 0.83 (d, 3H), 0.63 (t, 3H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 159.3, 141.0, 138.0, 132.1, 130.6, 130.5, 129.9, 126.6, 121.8, 112.3, 66.0, 56.1, 55.4, 54.5, 44.2, 38.6, 25.3, 24.3, 22.8, 20.8, 18.2, 14.0. ESI calculated for $\text{C}_{26}\text{H}_{37}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 493; Observed: 493.
- 10

EXAMPLE 216**4-chloro-N-(cyclopropylmethyl)-N-{2-[3-(1-piperidinyloxy)benzyl]benzenesulfonamide hydrochloride**

- 15 $R_f = 0.25$ (5% methanol, 1% triethylamine in DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.84 (d, 2H), 7.62 (d, 2H), 7.30 (dt, 1H), 7.21 (dd, 2H), 6.98 (d, 1H), 6.94 (t, 2H), 4.42 (s, 2H), 4.13 (t, 2H), 3.63 (d, 2H), 3.51-4.46 (m, 2H), 3.02 (t, 2H), 2.88 (d, 2H), 2.34-2.28 (m, 2H), 1.94-1.79 (m, 5H), 1.69-1.49 (m, 1H), 0.61-0.54 (m, 1H), 0.24-0.21 (m, 2H), (-)0.12-(-)0.14 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ 158.6, 140, 139.4, 132.2, 130.9, 130.6, 130.0, 125.1, 121.8, 112.4, 66.0, 56.1, 54.4, 53.8, 50.0, 25.3, 24.3, 22.8, 11.28, 4.7. ESI calculated for $\text{C}_{25}\text{H}_{33}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 477; Observed: 477.
- 20

EXAMPLE 217

4-chloro-N-(5-hexynyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride

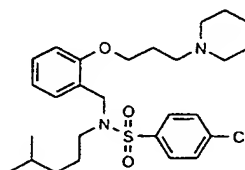


$R_f = 0.19$ (1% triethylamine/5% methanol/ethyl acetate) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.86-7.83 (m, 2H), 7.66-7.31 (m, 2H), 7.36-7.31 (m, 2H), 7.22-7.19 (m, 1H), 7.10-7.09 (m, 1H), 7.00-6.92 (m, 2H), 4.41 (s, 2H), 4.15 (t, 2H), 3.33 (m, 2H), 2.99 (m, 2H), 2.34-2.24 (m, 2H), 2.17 (t, 1H), 1.93-1.68 (m, 8H), 1.22-1.15 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 159.1, 140.6, 139.2, 133.0, 131.6, 131.1, 130.5, 125.03, 122.2, 112.8, 85.1, 70.3, 66.3, 56.5, 54.9, 50.9, 29.4, 26.9, 25.7, 24.7, 23.2, 18.9. ESI calculated for $\text{C}_{27}\text{H}_{35}\text{N}_2\text{O}_3\text{ClS}$ $[\text{MH}^+]$ 503; Observed: 503.

10

EXAMPLE 218

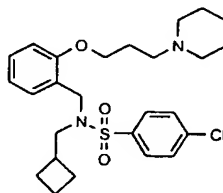
4-chloro-N-(4-methylpentyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



$R_f = 0.33$ (1% triethylamine/5% methanol/ethyl acetate) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.86-7.83 (m, 2H), 7.66-7.63 (m, 2H), 7.36-7.31 (m, 2H), 7.18 (m, 2H), 7.94 (dt, 2H), 4.36 (s, 2H), 4.14 (t, 2H), 3.67-3.51 (m, 4H), 3.07-2.90 (m, 4H), 2.30 (m, 2H), 2.00-1.50 (m, 6H), 0.84 (m, 2H), 0.68 (d, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 157.8, 139.3, 138.1, 131.8, 130.3, 129.9, 129.3, 123.9, 120.9, 111.5, 55.4, 53.8, 49.7, 48.6, 35.9, 27.8, 26.9, 24.6, 23.5, 22.0.

EXAMPLE 219

4-chloro-N-(cyclobutylmethyl)-N-{2-[3-(1-piperidinyloxy)propoxy]benzyl}benzenesulfonamide hydrochloride

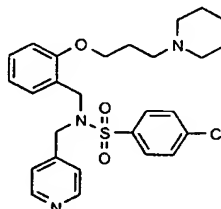


5 $R_f = 0.38$ (1% triethylamine/5% methanol/ethyl acetate) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.67 (d, 2H), 7.47 (d, 2H), 7.18-7.01 (m, 2H), 6.82-6.72 (m, 2H), 4.13 (s, 2H), 3.95 (t, 2H), 3.47 (m, 2H), 3.33 (m, 2H), 2.83 (m, 4H), 2.11 (m, 2H), 1.93-1.07 (m, 13H). ^{13}C NMR (75 MHz, CD_3OD) δ 158.6, 140.2, 138.7, 132.5, 131.1, 130.7, 130.3, 125.2, 121.8, 112.4, 66.0, 56.2, 55.01, 54.7, 51.0, 36.1, 27.1, 25.5, 24.4, 22.9, 18.6. ESI calculated for $\text{C}_{26}\text{H}_{35}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 491; Observed: 591.

10

EXAMPLE 220

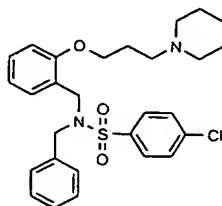
4-chloro-N-{2-[3-(1-piperidinyloxy)propoxy]benzyl}-N-(4-pyridinylmethyl)benzenesulfonamide dihydrochloride



15 $R_f = 0.23$ (5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.86-7.82 (br, 2H), 7.22-7.18 (br, 2H), 6.97-6.89 (br, 4H), 6.38-6.32 (br, 2H), 6.0-5.83 (br, 2H), 4.55 (br, 4H), 3.81-3.65 (m, 4H), 3.35-3.25 (m, 2H), 2.97-2.85 (m, 4H), 2.35-2.2.8 (m, 2H), 1.64-1.61 (br, 2H), 1.22-1.06 (m, 5H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 161.7, 158.5, 142.02, 140.9, 137.5, 132.0, 126.9, 123.4, 121.9, 112.1, 66.2, 56.2, 54.9, 54.8, 52.6, 52.0, 25.5, 24.4, 22.9.

EXAMPLE 221

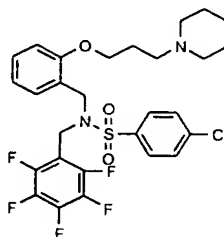
N-benzyl-4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



$R_f = 0.24$ (1% triethylamine/5% methanol/ethyl acetate) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.64 (d, 2H), 7.40 (d, 2H), 7.05-6.86 (m, 5H), 6.70 (m, 2H), 6.58 (t, 1H), 6.47 (d, 1H), 4.19 (s, 2H), 3.98 (s, 2H), 3.68 (t, 2H), 3.38 (m, 2H), 3.18 (m, 2H), 2.75 (t, 2H), 1.99 (m, 2H), 1.89-1.14 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 159.6, 141.4, 140.3, 139.5, 133.8, 132.3, 131.9, 131.4, 130.4, 130.2, 129.4, 125.2, 122.8, 113.3, 66.9, 57.5, 55.9, 53.7, 51.5, 26.5, 25.6, 24.0.

EXAMPLE 222

4-chloro-N-(2,3,4,5,6-pentafluorobenzyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride

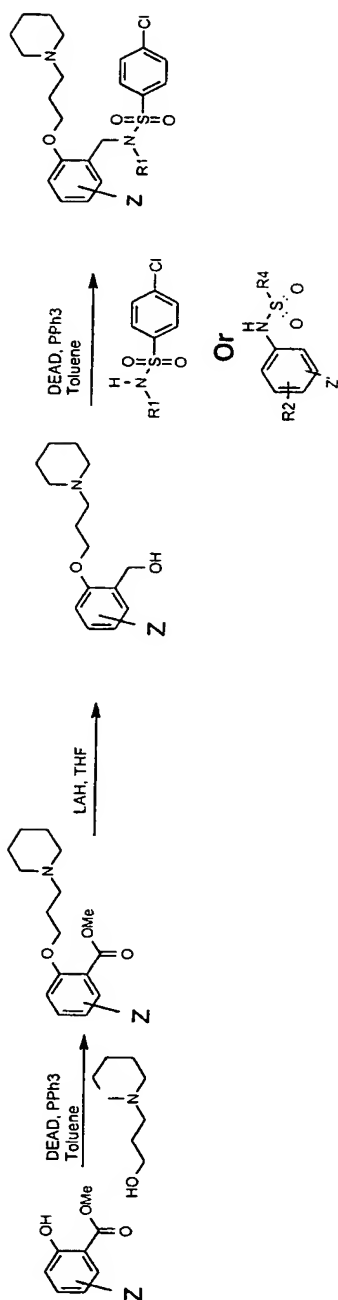


$R_f = 0.29$ (1% triethylamine/5% methanol/ethyl acetate) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.91-7.87 (m, 2H), 7.01-7.67 (m, 2H), 7.14 (m, 2H), 6.76 (m, 2H), 4.36 (d, 4H), 3.99 (d, 2H), 3.61-3.47 (m, 4H), 3.03 (m, 2H), 2.28 (m, 2H), 1.93-1.54 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 157.9, 140.5, 137.6, 133.3, 130.9, 130.6, 130.0, 127.5, 121.2, 111.2, 65.5, 55.8, 54.2, 51.1, 41.5, 24.9, 24.1, 22.5. ESI calculated for $\text{C}_{28}\text{H}_{28}\text{ClF}_5\text{N}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 603; Observed: 603.

EXAMPLE 223

The general reaction scheme outlined in **Scheme 223** is described in detail in the text following the scheme..

5

SCHEME 223

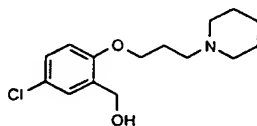
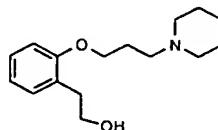
2-(3'-Piperidinylpropyloxy)-methyl benzoate

To a solution of methylsalicylate (15.0 g, 98.8 mmol) in dry benzene (300 mL) was added Triphenylphosphine (25.8 g, 98.8 mmol) followed by N-(3-hydroxypropyl) piperidine (14.12g, 98.8 mmol). The clear reaction mixture was cooled to 0 °C in an ice bath and DEAD (16.5 mL, 108.7 mmol) was added in drops over a period of 15 min. The reaction mixture was slowly warmed to room temperature and left stirred at room temperature for 15 h. The reaction mixture was filtered to remove the precipitated triphenylphosphineoxide and the filtrate was extracted with 1.0 M HCl (2 x 100 mL), the combined HCl solution was basified to pH 9 by the addition of solid NaHCO₃. The basic solution was extracted with ethyl acetate (3 x 100 mL). The combined ethyl acetate extracts were washed with saturated brine (2 x 75 mL), dried with MgSO₄, filtered and concentrated under reduced pressure to give 20.97 g of pale yellow oil (y: 77%) ¹H NMR (CDCl₃) δ (ppm): 7.70 (dd, 1.8 Hz, 1H), 7.42 (dt, 1.5 Hz, 1H), 6.99-6.94 (m, 2H), 4.08 (t, 2H), 3.88 (s, 3H), 2.58-2.45 9m, 6H), 2.04 (p, 2H), 1.65-1.60 (m, 4H), 1.47-1.45 (m, 2H).

2-(3'-Piperidinylpropyloxy)-benzylalcohol

To a suspension of lithium aluminum hydride (5.48 g, 144 mmol) in anhydrous THF (500 mL) was added a solution of the methyl ester (20 g, 72.1 mmol) in THF (200 mL) over a period of 30 min. The reaction mixture was refluxed for 6 h, cooled to 0 °C and quenched with water (5.48 mL) followed by 15% NaOH solution (5.48 mL) and finally with water (16.5 mL). The crystalline precipitate was filtered through the celite. The filtrate was concentrated to yield 18.9 g of crude product, which was purified by chromatography on SiO₂ (2% methanol in CHCl₃) to yield 17.98 g of product as white crystalline solid (y: 91%). ¹H NMR (CDCl₃) δ (ppm): 7.27-7.22 (m, 2H), 6.96-6.89 (m, 2H), 4.63 (s, 2H), 4.07 (t, J =, 2H), 2.55-2.40 (m, 6H), 2.00 (p, 2H), 1.66-1.58 (m, 4H), 1.46-1.43 (m, 2H).

The following compounds were similarly prepared.

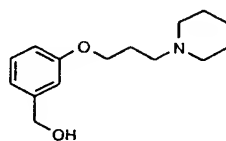
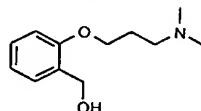
25 3-Chloro 6-(3'-piperidinylpropyloxy)-benzylalcohol.**2-(3'-Piperidinylpropyloxy)-phenethylalcohol.**

¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.23-7.12 (m, 2H), 6.90-6.83 (m, 2H), 4.05 (t, 2H), 3.83 (t, 2H), 2.91 (t, 3H), 2.51-2.47 (m, 6H), 1.99 (p, 2H), 1.72-1.58 (m, 4H), 1.48-1.40 (m, 2H).

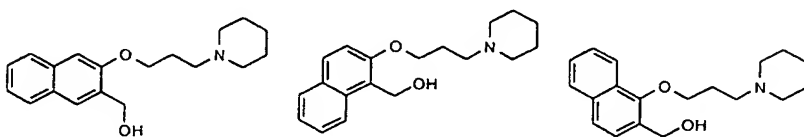
WO 00/50391

132

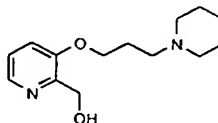
PCT/US00/04560

3-(3'-Piperidinyloxypropoxy)-benzylalcohol.**2-(3-N,N'-dimethylaminopropoxy)benzylalcohol.**

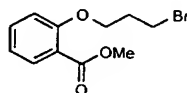
5

2-(3'-Piperidinyloxypropoxy)-β-naphthylalcohol.

10

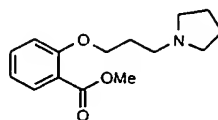
3-(3'-Piperidinyloxypropoxy)-2-hydroxymethyl pyridine.

¹H NMR (300 MHz, CDCl₃) δ (ppm): 8.14 (dd, 1H), 7.20-7.12 (m, 2H), 4.72 (s, 2H), 4.05 (t, 3H), 2.51-2.40 (m, 6H), 2.00 (p, 2H), 1.64-1.57 (m, 4H), 1.46-1.44 (m, 2H).

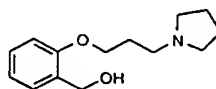
15 2(3-Bromopropoxy)methylbenzoate

20

To a stirred solution of methyl salicylate (4.0 g, 26.3 mmol) dry THF (100 mL) under Ar was added Triphenylphosphine (6.9g, 26.3 mmol) followed by 3-bromopropanol (3.66g, 26.3 mmol). The reaction mixture was cooled to 0 °C in an ice bath and DEAD (4.55 mL, 28.9 mmol) was added in drops over period of 15 min. The reaction mixture was left to stir at room temperature for 15h. The reaction mixture concentrated under reduced pressure. The resulting crude product was purified by chromatography over SiO₂ (10:1, hexanes/ethyl acetate) to give 4.5 g of the desired product as a pale yellow oil (y: 63%). ¹H NMR (CDCl₃) δ (ppm): 7.83-7.99 (dd, 1H), 7.49-7.44 (t, 1H), 7.00-6.97 (m, 2H), 4.19 (t, 2H), 3.89 (s, 3H), 3.71 (t, 2H), 2.36 (p, 2H).

2(3-Pyrrolidinylpropyloxy)methylbenzoate

2(3-Bromopropoxy)methylbenzoate (4.0 g, 11.3 mmol) was dissolved in neat pyrrolidine (40 mL) and stirred at room temperature for 1h. The reaction mixture was then concentrated under reduced pressure. The isolated residue re-dissolved in DCM and washed with saturated bicarbonate solution (2x 50 mL), dried with MgSO₄, filtered and concentrated under reduced pressure to give 3.8 g of colorless oil (y: 99%) ¹H NMR (CDCl₃) δ (ppm): 7.79-7.77 (d, 1H), 7.47 (t, 1H), 6.99-6.94 (m, 2H), 4.11 (t, 2H), 3.89 (s, 2H), 2.67 (t, 2H), 2.57 (br, 4H), 2.06 (p, 2H), 1.87 (br, 4H).

2-(3-Pyrrolidinylpropyloxy)benzylalcohol

To a suspension of lithium aluminum hydride (0.9 g, 23.6 mmol) in anhydrous THF (100 mL) was added a solution of the methyl ester (3.0 g 11.8 mmol) in THF (10 mL) over a period of 10 min. The reaction mixture was refluxed for 6 h, cooled to 0 °C and quenched with water (0.9 mL) followed by 15% NaOH solution (0.9 mL) and finally with water (2.7 mL of). The crystalline precipitate was filtered through the celite. The filtrate was concentrated to yield 2.3 g of crude product, which was subsequently purified by chromatography on SiO₂ (hexanes/ethyl acetate 5:1) to afford 2.02 g of product as colorless oil (y: 76%). ¹H NMR (CDCl₃) δ (ppm): 7.26-7.22 (m, 2H), 6.95-6.88 (m, 2H), 4.61 (s, 2H), 4.1 (t, 2H), 2.68 (t, 2H), 2.54 (br, 4H), 2.03 (p, 2H), 1.85-1.81 (m, 4H).

General procedure for the synthesis of 4-chlorobenzenesulfanilides

To 1.0 g of amine dissolved in DCM (20 mL) or 1, 2-dichloroethane was added 1.1 equivalent of pyridine and 1.0 equivalent of 4-chlorobenzenesulfonylchloride. The reaction mixture was gently refluxed over night then cooled to room temperature. The reaction mixture was concentrated under reduced pressure and the crude product was recrystallised from DCM/hexanes to give the product in 90-95 % yield.

General Procedure for the preparation of 4-chlorobenzenesulfonamides

To a biphasic mixture of alkylamines (1.0g) in water (20 mL) was added 1.6 equivalent of solid NaHCO₃ followed by 1.0 equivalent of 4-chlorobenzenesulfonamide. The heterogeneous mixture was refluxed for 2 h then cooled to room temperature and acidified with 1.0 M HCl to pH 1. The

precipitated product was filtered, washed with water and subsequently recrystallized from ethyl acetate/hexanes to give the crystalline sulfonamide in 85-95% yield.

General procedure for alkylation of 4-chlorobenzenesulfonamides

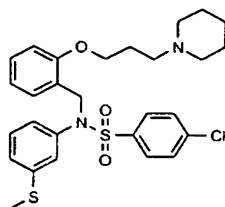
To a stirred solution of 2-(3'-piperidinyloxy)benzylalcohol (1.0 equivalent) in THF (10 mL/mmol) was added 1.5 equivalent of PPh_3 and 4-chlorobenzenesulfonamides followed by 1.5 equivalent of DEAD. The reaction mixture was stirred at room temperature for 12 h then concentrated under reduced pressure. The crude mixture was purified by chromatography (multiple elution 200 mL of ethyl acetate followed by 0.5 % methanol 0.5% triethylamine in ethyl acetate) to give 45-60 % yield of product as a colorless oil (free base). The free base was dissolved in DCM and an excess of a 1.0 M solution of HCl in ether was added. The resulting solution was concentrated under reduced pressure to give white solid. The HCl salt was purified by passing through a short column of silica and eluting with 10% methanol in DCM to yield white solid.

The following compounds were prepared according to the scheme described in the previous example.

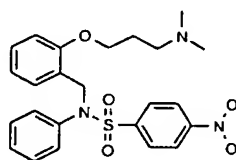
15

EXAMPLE 224

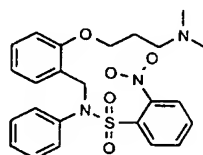
4-chloro-N-[3-(methylsulfonyl)phenyl]-N-{2-[3-(1-piperidinyloxy)propoxy]benzyl}benzenesulfonamide hydrochloride



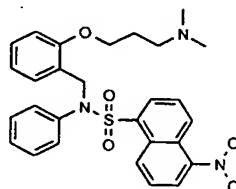
$R_f = 0.25$ (5% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.87-7.84 (m, 2H), 7.63-7.50 (m, 3H), 7.33-7.27 (m, 5H), 6.91 (m, 2H), 6.44 (m, 1H), 4.82 (d, 1H), 4.61 (m, 1H), 4.24 (m, 1H), 3.51 (s, 2H), 3.34 (m, 4H), 2.41 (t, 4H), 1.66-1.26 (m, 9H), 0.87 (m, 9H).

EXAMPLE 225**N-{2-[3-(dimethylamino)propoxy]benzyl}-4-nitro-N-phenylbenzenesulfonamide**

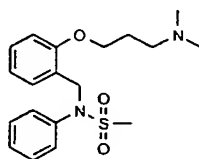
5 $R_f = 0.32$ (9% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 8.36-8.22 (m, 3H), 8.06 (m, 1H), 7.80 (m, 2H), 7.23-7.15 (m, 3H), 6.82-6.67 (m, 5H), 4.82 (s, 2H), 4.12 (t, 2H), 3.45 (m, 2H), 2.87 (s, 6H), 2.41 (m, 2H).

EXAMPLE 226**N-{2-[3-(dimethylamino)propoxy]benzyl}-2-nitro-N-phenylbenzenesulfonamide**

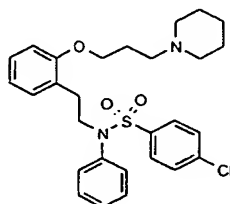
10 $R_f = 0.16$ (9% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.62 (m, 2H), 7.50-7.42 (m, 2H), 7.29-7.07 (m, 7H), 6.85-6.74 (m, 2H), 5.04 (s, 2H), 3.86 (t, 2H), 2.42 (t, 2H), 2.25 (s, 6H), 1.85 (m, 2H).

EXAMPLE 227**5-(dimethylamino)-N-{2-[3-(dimethylamino)propoxy]benzyl}-N-phenyl-1-naphthalenesulfonamide**

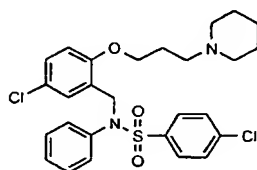
15 $R_f = 0.16$ (9% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 8.69-8.23 (m, 15H), 4.99 (s, 2H), 4.12 (t, 2H), 3.60 (m, 2H), 2.85 (s, 6H), 2.50 (m, 2H).

EXAMPLE 228**N-{2-[3-(dimethylamino)propoxy]benzyl}-N-phenylmethanesulfonamide**

5 $R_f = 0.16$ (9% methanol/DCM) $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.33-7.15 (m, 6H), 6.91-6.70 (m, 3H), 4.88 (s, 2H), 4.06 (t, 2H), 3.36 (t, 2H), 2.97 (s, 3H), 2.82 (s, 6H), 2.48-2.37 (m, 2H).

EXAMPLE 229**4-chloro-N-phenyl-N-(2-{2-[3-(1-piperidiny)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride**

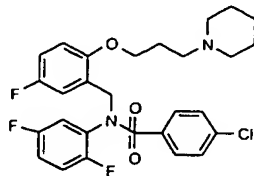
10 $R_f = 0.17$ (5% methanol, 1% triethylamine) $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.54-7.47 (m, 4H), 7.36-7.34 (m, 2H), 7.17 (dt, 1H), 7.04 (m, 2H), 6.92 (m, 2H), 6.75 (t, 1H), 4.17-4.05 (m, 2H), 3.86-3.81 (m, 2H), 3.6 (br, 2H), 3.45-3.40 (m, 2H), 3.1 (BR, 2H), 2.79-2.74 (m, 2H), 2.34-2.25 (m, 2H), 1.88 (br, 4H), 1.25 (t, 2H). ESI calculated for $\text{C}_{28}\text{H}_{33}\text{ClN}_2\text{O}_3\text{S}$ (MH⁺) 513, Observed 513.

EXAMPLE 230**4-chloro-N-{5-chloro-2-[3-(1-piperidiny)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride**

15 $R_f = 0.43$ (3:1:1; nBuOH:H₂O:AcOH). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.59-7.53 (m, 4H), 7.20-7.17 (m, 3H), 7.10 (dd, 1H), 6.90-6.83 (m, 4H), 4.81 (s, 2H), 4.08 (t, 2H), 3.56-3.50 (m, 4H), 3.06-3.03
20 (br, 2H), 2.31-2.26 (m, 2H), 1.94-1.80 (m, 6H).

EXAMPLE 231

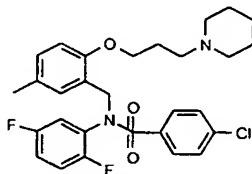
4-chloro-N-(2,5-difluorophenyl)-N-{5-fluoro-2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



5 $R_f = 0.47$ (9 % methanol in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.74 (d, 2H), 7.65 (d, 2H), 7.10-8.05 (m, 2H), 6.99-6.89 (m, 2H), 6.85-6.75 (m, 2H), 4.83 (s, 2H), 4.11 (t, 2H), 3.41 (m, 2H), 3.21 (br, 2H), 2.32-2.23 (m, 2H), 1.87 (m, 4H), 1.58 (br, 2H). LC-MS calculated for $\text{C}_{27}\text{H}_{28}\text{ClF}_3\text{N}_2\text{O}_3\text{S}$, $[\text{MH}^+]$ 553; Observed: 553.

EXAMPLE 232

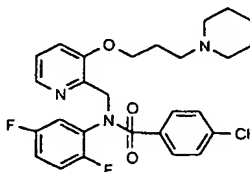
10 **4-chloro-N-(2,5-difluorophenyl)-N-{5-methyl-2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**



15 $R_f = 0.45$ (9 % methanol in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.75 (d, 2H), 7.66 (d, 2H), 7.05 (m, 3H), 6.81 (m, 3H), 4.76 (s, 2H), 4.03 (t, 2H), 3.13-3.00 (m 6H), 2.18 (m, 5H), 1.82 (m, 4H), 1.67 (m, 2H).

EXAMPLE 233

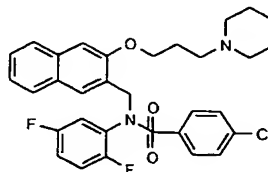
4-chloro-N-(2,5-difluorophenyl)-N-({3-[3-(1-piperidinyl)propoxy]-2-pyridinyl}methyl)benzenesulfonamide hydrochloride



20 $R_f = 0.33$ (10% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.71 (d, 1H), 7.63-7.51 (m, 4H), 7.31 (d, 1H), 7.15 (m, 1H), 6.90 (m, 2H), 6.62 (m, 1H), 4.87 (s, 2H), 4.08 (t, 2H), 3.28 (m, 2H), 3.07 (m, 4H), 2.21 (m, 2H), 1.74 (m, 4H), 1.55 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 157.1, 146.0, 142.9, 142.5, 139.9, 132.3, 132.1, 129.3, 129.1, 129.0, 127.9, 122.2, 121.7, 121.3, 120.3, 120.1, 120.0, 119.8, 58.5, 57.8, 56.4, 54.3, 27.2, 26.4, 25.0.

EXAMPLE 234

4-chloro-N-(2,5-difluorophenyl)-N-({3-[3-(1-piperidiny)propoxy]-2-naphthyl}methyl)benzenesulfonamide hydrochloride

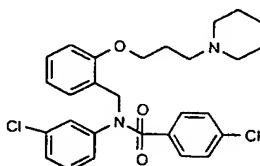


5 $R_f = 0.55$ (9% methanol/DCM) ^1H NMR (500 MHz, CD_3OD) δ (ppm): 7.73-7.67 (dd, 4H), 7.63-7.55 (dd, 3H), 7.43 (s, 1H), 7.38 (m, 1H), 7.24 (t, 1H), 7.18 (s, 1H), 6.95 (m, 2H), 6.81 (m, 1H), ^{13}C NMR (125 MHz, CD_3OD) δ (ppm): 160.3, 159.1, 158.4, 156.5, 141.0, 138.5, 136.3, 132.4, 130.8, 130.5, 129.7, 128.62, 128.0, 127.7, 125.3, 125.2, 120.0, 119.8, 118.4, 118.4, 118.2, 118.2, 107.3, 66.7, 56.7, 55.0, 51.5, 26.0, 25.1, 23.7.

10

EXAMPLE 235

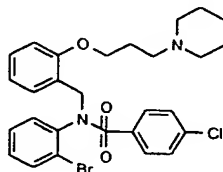
4-chloro-N-(3-chlorophenyl)-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride



15 $R_f = 0.13$ (1% triethylamine/ethyl acetate) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.61 (m, 4H), 7.17 (m, 3H), 6.92-6.84 (m, 4H), 6.67 (t, 1H), 4.84 (s, 2H), 4.15 (br, 2H), 3.67 (m, 4H), 3.06 (t, 2H), 2.34 (br, 2H), 2.02-1.52 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 156.5, 140.3, 139.4, 136.6, 134.0, 130.1, 129.6, 129.2, 129.0, 128.6, 128.0, 127.0, 123.2, 120.4, 111.0, 66.4, 56.0, 54.6, 48.7, 26.7, 26.0, 24.4.

EXAMPLE 236

20 **4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1-piperidiny)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride**

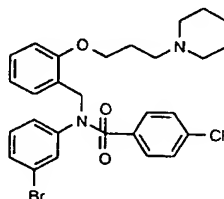


$R_f = 0.19$ (1% triethylamine/ethyl acetate) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.66 (dd, 4H), 7.45 (d, 1H), 7.15 (m, 3H), 6.85 (dd, 2H), 7.67 (d, 1H), 6.58 (t, 1H), 5.20 (d, 1H), 4.53 (d, 1H),

4.19-4.05 (m, 2H), 3.83 (m, 3H), 3.31 (br, 2H), 2.33 (br, 2H), 2.00-1.78 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 156.5, 140.3, 139.4, 136.6, 134.0, 130.1, 129.6, 129.1, 128.6, 128.0, 127.0, 123.2, 120.4, 111.0, 56.0, 54.6, 48.7, 26.7, 26.0, 24.4.

EXAMPLE 237

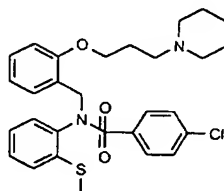
5 **N-(3-bromophenyl)-4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**



$R_f = 0.59$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.42 (m, 2H), 7.45 (m, 1H), 7.22-7.06 (m, 3H), 6.93-6.84 (m, 3H), 6.68 (t, 1H), 4.85 (s, 2H), 4.27 (t, 2H), 3.61 (m, 4), 3.07 (br, 2H), 2.34 (m, 2H), 1.92 (m, 6H).

EXAMPLE 238

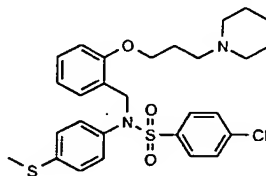
4-chloro-N-[2-(methylsulfanyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



15 ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.72-7.75 (m, 2H), 7.65-7.59 (m, 2H), 7.32-7.10 (m, 3H), 6.97 (dt, 1H), 6.85 (d, 1H), 6.69 (d, 1H), 6.57 (dt, 1H), 5.20 (d, 1H), 4.17 (m, 1H), 3.99 (m, 1H), 3.53 (m, 1H), 3.20 (m, 4H), 2.23 (m, 2H), 2.12 (s, 3H), 1.91 (m, 4H), 1.65 (br, 2H). ESI calculated for $\text{C}_{28}\text{H}_{33}\text{ClN}_2\text{O}_3\text{S}_2$ $[\text{MH}^+]$ 545; Observed: 545.

EXAMPLE 239

4-chloro-N-[4-(methylsulfanyl)phenyl]-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride

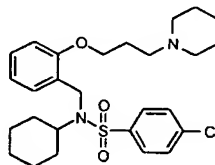


5 $R_f = 0.40$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.60 (m, 4H), 7.16 (m, 1H), 7.03 (m, 2H), 6.85-6.77 (m, 3H), 6.66 (m, 1H), 4.81 (s, 2H), 4.10 (m, 4H), 3.06 (m, 2H), 2.39-2.28 (m, 5H), 2.02-1.1.28 (m, 8H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 156.4, 139.1, 138.5, 136.9, 135.8, 130.0, 129.1, 129.1, 129.1, 128.8, 126.1, 123.7, 120.4, 111.0, 66.3, 56.0, 55.8, 54.6, 48.9, 26.7, 26.0, 25.7, 24.4, 15.3, 14.5, 14.2.

10

EXAMPLE 240

4-chloro-N-cyclohexyl-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride

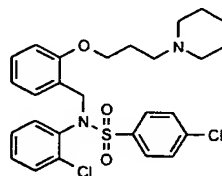


15 $R_f = 0.49$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.84-7.82 (m, 2H), 7.61-7.58 (m, 2H), 7.14-7.25 (m, 2H), 6.97-6.89 (m, 2H), 4.53 (s, 2H), 4.15 (m, 2H), 3.63-3.43 (m, 4H), 2.99 (m, 2H), 2.29 (m, 2H), 1.98-1.12 (m, 16H). ^{13}C NMR (75 MHz, CD_3OD) δ : 158.1, 141.3, 140.0, 131.6, 130.7, 130.3, 129.8, 127.1, 121.7, 112.4, 66.1, 59.9, 56.1, 54.5, 44.8, 32.4, 27.3, 26.4, 25.3, 24.4, 22.8.

EXAMPLE 241

4-chloro-N-(2-chlorophenyl)-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride

20

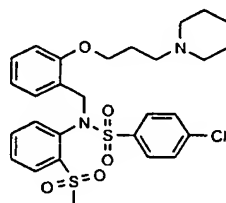


$R_f = 0.44$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.73-7.69 (m, 2H), 7.64-7.59 (m, 2H), 7.30-7.10 (m, 4H), 6.90-6.80 (m, 3H), 6.64 (dt, 1H), 5.07 (d, 1H), 4.70 (d, 1H), 4.12-3.99 (d, 2H), 3.52 (m, 1H), 3.17 (b, 4H), 2.21 (br, 2H), 1.84 (m, 4H), 1.65 (m, 2H) ^{13}C NMR (75

MHz, CD₃OD) δ (ppm): 156.9, 139.0, 138.7, 135.7, 134.8, 133.4, 134.0, 130.3, 129.5, 129.3, 129.1, 129.0, 127.0, 123.6, 120.2, 110.9, 66.3, 55.9, 54.6, 48.5, 26.5, 26.0, 24.4.

EXAMPLE 242

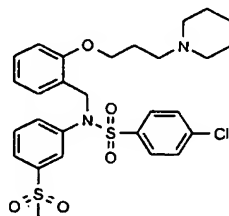
4-chloro-N-[2-(methylsulfonyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



$R_f = 0.13$ (0.2% triethylamine/5% methanol/ethyl acetate) ¹H NMR (300 MHz, CD₃OD) δ (ppm): 8.07 (dd, 1H), 7.78-7.4 (m, 2H), 7.66-7.45 (m, 1H), 7.17 (m, 1H), 6.80 (m, 2H), 6.64 (m, 2H), 5.24 (d, 1H), 4.63 (d, 1H), 3.88 (m, 1H), 3.70 (m, 1H), 3.06 (m, 9H), 1.99 (m, 2H), 1.80 (m, 4H), 1.63 (m, 2H).

EXAMPLE 243

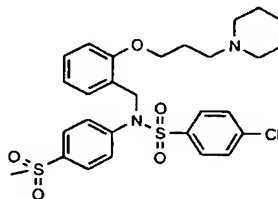
4-chloro-N-[3-(methylsulfonyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



$R_f = 0.19$ (5% methanol 0.2 %triethylamine in ethyl acetate). ¹H NMR (CD₃OD) δ (ppm): 7.78-7.75 (m, 1H), 7.61 (m, 4H), 7.47 (t, 1H), 7.42 (t, 1H), 7.35-7.32 (ddd, 1H), 7.17-7.11 (dt, 1H), 7.04-7.01 (dd, 1H), 6.86 (d, 1H), 6.71 (dt, 1H), 4.87 (s, 2H), 4.02 (t, 2H), 3.14-3.09(m, 2H), 2.97-2.95 (s overlaps m, 5H), 2.18-2.12 (m, 2H), 1.82-1.74 (m, 4H), 1.62-1.60 (m, 2H).

EXAMPLE 244

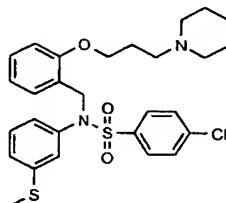
4-chloro-N-[4-(methanesulfonyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



5 $R_f = 0.18$ (93:5:2;ethyl acetate:methanol:triethylamine). ^1H NMR (300 MHz, CD_3OD) δ :7.79 (d, 2H), 7.62 (m, 4H), 7.27-7.14 (m, 3H), 6.96-6.88 (m, 2H), 6.69 (m, 1H), 4.9 (s overlapped by HOD), 2H), 4.12 (m, 2H), 3.70-3.59 (m, 4H), 3.07-3.01 (m overlaps s, 5H), 2.29 (m, 2H), 2.02-1.78 (m, 6H). ESI calculated for $\text{C}_{28}\text{H}_{33}\text{ClN}_2\text{O}_5\text{S}_2$: 576 . Observed 577 (MH+).

EXAMPLE 245

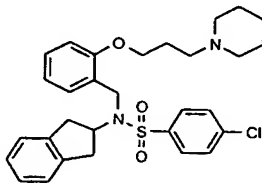
10 **4-chloro-N-[3-(methanesulfonyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**



^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.62 (m, 4H), 7.32-7.05 (m, 3H), 6.95-6.82(m, 2H), 6.92-6.61 (m, 3H), 4.84 (s, 2H), 4.14 (t, 2H), 3.58 (m, 4H), 3.05 (m, 2H), 2.28 (m, 5H), 1.88 (br, 6H).
15 ESI calculated for $\text{C}_{28}\text{H}_{33}\text{ClN}_2\text{O}_5\text{S}_2$ [MH+] 545; Observed: 545.

EXAMPLE 246

4-chloro-N-(2,3-dihydro-1H-inden-2-yl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride

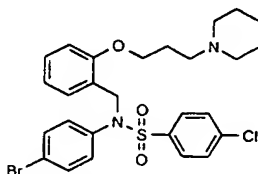


20 $R_f = 0.24$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.91-7.87 (m, 2H), 7.64-7.61 (m, 2H), 4.78 (m, 1H), 7.21 (m, 1H), 7.05-6.90 (m, 5H), 6.83 (d, 1H), 4.88 (m, 1H), 4.43 (s, 2H), 3.88 (t, 2H), 3.30 (m, 2H), 2.88-2.59 (m, 10H), 1.67-1.50 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ

(ppm): 157.1, 141.4, 140.8, 140.3, 130.8, 130.3, 130.2, 129.7, 127.9, 127.5, 125.3, 121.7, 112.01, 66.8, 60.0, 56.8, 55.2, 43.6, 37.2, 26.6, 25.8, 24.4.

EXAMPLE 247

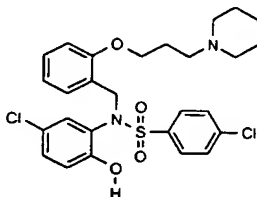
N-(4-bromophenyl)-4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



$R_f = 0.18$ (19:1 DCM:methanol) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.71 (m, 4H), 7.33 (m, 2H), 7.17 (m, 1H), 6.91-6.81 (m, 4H), 6.69 (m, 1H), 4.82 (s, 2H), 4.10 (t, 2H), 3.56 (m, 2H), 3.23 (m, 4H), 2.28 (m, 2H), 1.86 (m, 4H), 1.66 (br, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.5, 140.7, 138.9, 137.8, 133.1, 132.2, 131.1, 130.7, 130.6, 124.0, 122.9, 121.5, 112.3, 66.2, 56.4, 54.9, 51.4, 25.7, 24.8, 23.2.

EXAMPLE 248

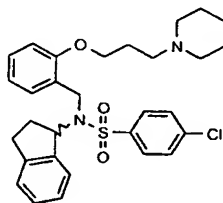
4-chloro-N-(5-chloro-2-hydroxyphenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



$R_f = 0.62$ (10% methanol/DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.68-7.65 (m, 2H), 7.56-7.53 (m, 2H), 7.21-7.16 (m, 1H), 7.0 (dd, 1H), 6.92-6.87 (m, 2H), 6.76 (d, 1H), 6.67 (t, 1H), 6.56 (d, 1H), 4.93 (s, 2H), 4.15 (t, 2H), 3.72-3.60 (m, 4H), 3.12-3.10 (m, 2H), 2.39-2.30 (m, 2H), 2.04-1.73 (m, 5H), 1.61-1.52 (m, 1H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.4, 155.4, 140.2, 139.6, 133.9, 132.7, 131.1, 130.7, 130.4, 130.2, 125.9, 124.5, 124.1, 121.5, 118.2, 112.1, 65.9, 56.2, 54.7, 25.5, 24.5, 22.9.

EXAMPLE 249

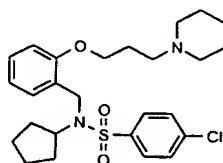
4-chloro-N-(2,3-dihydro-1H-inden-1-yl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



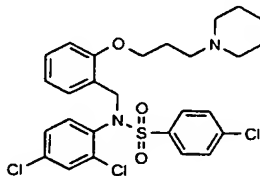
- 5 $R_f = 0.40$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.89 (m, 2H), 7.60 (m, 2H), 7.31 (d, 1H), 7.23-7.07 (m, 3H), 6.91 (m, 1H), 6.80 (t, 1H), 6.71 (d, 1H), 6.56 (d, 1H), 5.57 (t, 1H), 4.49 (d, 1H), 4.12 (m, 1H), 3.80 (t, 2H), 2.86-2.45 (m, 8H), 2.17 (m, 1H), 1.91-1.70 (m, 3H), 1.66-1.49 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 157.6, 145.2, 141.3, 140.8, 140.2, 130.8, 130.7, 130.1, 129.6, 129.36, 127.4, 127.1, 126.1, 125.8, 121.3, 111.8, 67.0, 65.0, 57.1, 55.5, 43.8, 31.5, 31.0, 27.0, 26.3, 25.0.
- 10

EXAMPLE 250

4-chloro-N-cyclopentyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride

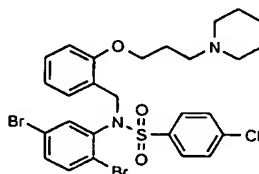


- 15 $R_f = 0.60$ (9:1; DCM:methanol) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.84 (m, 2H), 7.73-7.62 (m, 2H), 7.37 (d, 1H), 7.25 (m, 1H), 6.93 (m, 2H), 4.45 (s, 2H), 4.25 (m, 2H), 4.11 (t, 2H), 2.28 (m, 2H), 2.00-1.71 (m, 4H), 1.56-0.87 (m, 10H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 157.2, 140.8, 140.0, 133.2, 133.06, 130.6, 130.5, 130.1, 130.0, 129.8, 127.6, 121.8, 112.2, 66.1, 60.8, 55.9, 54.5, 44.2, 29.86, 25.3, 24.4, 22.8.

EXAMPLE 251**4-chloro-N-(2,4-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**

5 $R_f = 0.31$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.65-7.52 (m, 4H), 7.28 (d, 1H), 7.14-7.07 (m, 2H), 6.79 (m, 3H), 6.60 (t, 1H), 4.96 (m, 1H), 4.60 (m, 1H), 4.00 (m, 2H), 3.34-3.03 (m, 6H), 2.10 (m, 2H), 1.73 (m, 4H), 1.55 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 160.34, 142.46, 140.79, 139.54, 137.77, 137.42, 136.15, 134.59, 132.99, 132.84, 132.39, 132.26, 130.38, 125.17, 123.08, 113.86, 67.96, 58.22, 56.55, 52.47, 27.56, 26.65, 25.19.

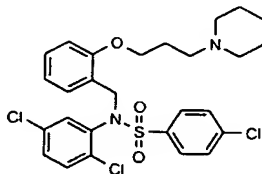
10

EXAMPLE 252**4-chloro-N-(2,5-dibromophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**

15 $R_f = 0.26$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.64-7.53 (m, 4H), 7.31 (d, 1H), 7.21 (dd, 1H), 7.10 (dt, 1H), 6.86 (d, 1H), 6.79 (d, 1H), 6.61 (t, 1H), 5.40 (d, 1H), 4.58 (d, 1H), 3.95 (m, 2H), 3.22-2.02 (m, 6H), 2.08 (m, 2H), 2.11-1.54 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 154.6, 136.9, 135.6, 134.4, 132.0, 130.2, 129.0, 127.4, 126.7, 126.7, 122.5, 118.9, 117.4, 117.33, 108.0, 61.7, 52.2, 50.6, 50.5, 21.3, 20.3, 18.7. ESI calculated for $\text{C}_{27}\text{H}_{29}\text{Br}_2\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 657; Observed: 657.

EXAMPLE 253

4-chloro-N-(2,5-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride

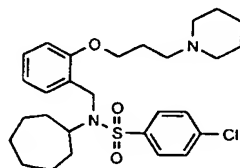


5 $R_f = 0.35$ (10% methanol/ CDCl_3) ^1H NMR (300 MHz, CD_3OD), δ (ppm): 7.72-7.60 (m, 4H), 7.27-7.15 (m, 3H), 6.87 (m, 2H), 6.78 (dd, 1H), 6.63 (t, 1H), 5.03 (d, 1H), 5.68 (d, 1H), 4.15 (m, 1H), 4.02 (m, 1H), 3.67 (m, 1H), 3.65 (m, 1H), 2.31 (m, 2H), 1.88 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.69, 141.00, 138.84, 137.78, 135.68, 133.50, 133.39, 133.02, 132.61, 131.54, 131.27, 130.82, 130.70, 123.27, 121.54, 112.23, 65.98, 56.28, 54.66, 51.00, 25.44, 24.42, 22.93.

10

EXAMPLE 254

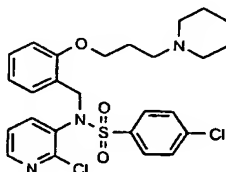
4-chloro-N-cycloheptyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



15 $R_f = 0.37$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.65 (d, 2H), 7.41 (d, 2H), 7.29 (d, 1H), 7.06 (t, 1H), 6.76 (m, 2H), 4.26 (s, 2H), 3.88 (t, 2H), 3.67 (m, 1H), 2.54-2.40 (m, 6H), 1.88 (m, 2H), 1.49-1.12 (m, 18H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.2, 141.9, 140.6, 131.7, 131.3, 130.6, 130.4, 128.5, 122.3, 112.9, 68.1, 62.6, 58.0, 56.2, 44.0, 35.3, 29.2, 28.0, 27.1, 27.0, 25.6,

EXAMPLE 255

20 **4-chloro-N-(2-chloro-3-pyridinyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**

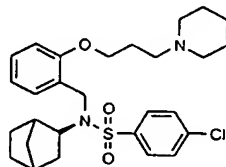


$R_f = 0.37$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.77-7.73 (4H, m), 7.33-7.20 (3H, m), 6.94-6.90 (m, 3H), 6.75-6.70 (m, 1H), 5.03 (d, 1H), 5.77 (d, 1H), 4.13-4.02 (m,

2H), 3.44-3.16 (m, 6H), 2.24 (m, 2H), 1.89-1.84 (m, 4H), 1.67 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 159.1, 141.0, 139.3, 138.6, 135.2, 133.4, 131.6, 131.6, 131.1, 134.0, 129.4, 127.8, 123.7, 121.6, 112.4, 66.1, 56.7, 54.9, 54.9, 51.6, 25.7, 24.7, 23.2.

EXAMPLE 256

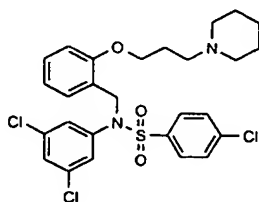
N-[(2S)-bicyclo[2.2.1]hept-2-yl]-4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



$R_f = 0.33$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.86-7.81 (m, 2H), 7.62-7.58 (m, 2H), 7.49 (m, 1H), 7.19 (m, 1H), 6.93 (m, 2H), 4.44 (s, 2H), 4.03 (m, 2H), 3.89 (m, 1H), 2.62 (m, 6H), 2.07-0.90 (m, 18H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.2, 142.3, 141.5, 132.1, 131.5, 131.3, 130.79, 129.4, 123.0, 113.5, 68.6, 64.2, 58.6, 56.9, 44.9, 43.5, 40.0, 38.6, 38.5, 31.8, 29.9, 28.66, 27.6, 26.3.

EXAMPLE 257

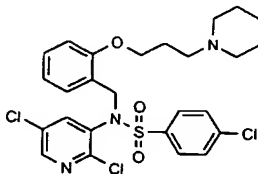
4-chloro-N-(3,5-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



$R_f = 0.6$ (10% methanol/DCM) ^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.65 (m, 4H), 7.30 (t, 1H), 7.23-7.18 (m, 1H), 6.98-6.92 (m, 4H), 6.73 (m, 1H), 4.15 (t, 2H), 3.64-3.57 (m, 2H), 3.70-3.67 (m, 2H), 3.09-3.04 (m, 2H), 2.38-2.32 (m, 2H), 2.10-1.98 (m, 2H), 1.88-1.79 (m, 4H). ESI calculated for $\text{C}_{27}\text{H}_{29}\text{Cl}_3\text{N}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 569; Observed: 569.

EXAMPLE 258

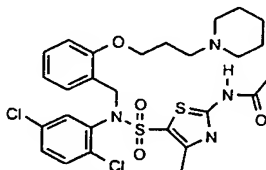
4-chloro-N-(2,5-dichloro-3-pyridinyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride



- 5 $R_f = 0.49$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 8.28 (d, 1H), 7.77-7.54 (m, 4H), 7.41 (d, 1H), 7.23 (m, 1H), 6.93-6.86 (m, 2H), 6.71 (m, 1H), 5.05 (m, 1H), 4.78 (m, 1H), 4.17-4.04 (m, 2H), 3.69-3.44 (m, 4H), 3.04 (m, 2H), 2.31 (m, 2H), 2.00-1.51 (m, 6H). ESI calculated for $\text{C}_{26}\text{H}_{28}\text{Cl}_3\text{N}_3\text{O}_3\text{S}$ $[\text{MH}^+]$ 568; Observed: 568.

EXAMPLE 259

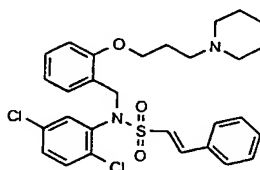
- 10 **N-{5-[(2,5-dichloro{2-[3-(1-piperidinyl)propoxy]benzyl}anilino)sulfonyl]-4-methyl-1,3-thiazol-2-yl}acetamide hydrochloride**



- 15 $R_f = 0.70$ (3:1:1 n-BuOH/ H_2O /AcOH) ^1H NMR (500 MHz, DMSO) δ (ppm): 12.73 (s, 1H), 10.08 (br, 1H), 7.43 (m, 2H), 7.27 (d, 1H), 7.20 (m, 1H), 6.99 (d, 1H), 6.91 (d, 1H), 6.75 (t, 1H), 4.99 (d, 1H), 4.69 (d, 1H), 4.00 (m, 2H), 3.47-3.22 (m, 11H), 2.21-1.70 (m, 9H). ESI calculated for $\text{C}_{27}\text{H}_{32}\text{Cl}_2\text{N}_4\text{O}_4\text{S}$ $[\text{MH}^+]$ 611; Observed: 611

EXAMPLE 260

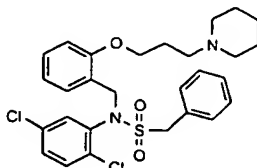
(E)-N-(2,5-dichlorophenyl)-2-phenyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}ethenesulfonamide hydrochloride



- 20 $R_f = 0.62$ (3:1:1 n-BuOH/ H_2O /AcOH) ^1H NMR (500 MHz, CD_3OD) δ (ppm): 7.62 (m, 2H), 7.45 (m, 3H), 7.35-7.32 (dd, 2H), 7.29-7.21 (m, 4H), 6.93 (m, 2H), 6.72 (t, 1H), 4.88 (m, 2H), 4.17 (m, 1H), 4.04 (m, 1H), 3.39 (m, 6H), 2.27 (m, 2H), 1.93 (m, 4H), 1.69 (m, 2H). ESI calculated for $\text{C}_{29}\text{H}_{32}\text{Cl}_2\text{N}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 559; Observed: 559.

EXAMPLE 261

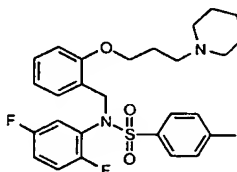
N-(2,5-dichlorophenyl)(phenyl)-N-{2-[3-(1-piperidiny)propoxy]benzyl}methanesulfonamide hydrochloride



5 $R_f = 0.67$ (3:1:1 n-BuOH/H₂O/AcOH) ¹H NMR (500 MHz, CD₃OD) δ (ppm): 7.39-7.28 (m, 8H), 6.96 (m, 2H), 6.80 (t, 2H), 4.88 (m, 2H), 4.51 (s, 2H), 4.05 (d, 2H), 3.31-3.30 (m, 6H), 2.18 (m, 2H), 1.78 (m, 4H), 1.61 (br, 2H). ESI calculated for C₂₈H₃₂Cl₂N₂O₃S [MH⁺] 547; Observed: 547.

EXAMPLE 262

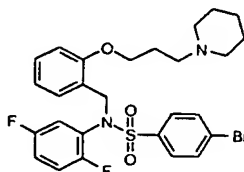
N-(2,5-difluorophenyl)-4-methyl-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride



10 ¹H NMR (300 MHz, CD₃OD) δ (ppm): 7.62-7.50 (m, 3H), 7.37 (m, 2H), 7.13 (t, 1H), 6.93-6.84 (m, 2H), 6.76 (d, 1H), 6.63-6.58 (m, 2H), 4.71 (s, 2H), 4.12-4.05 (m, 2H), 3.63-3.57 (m, 2H), 3.03 (t, 2H), 2.42 (s, 3H), 2.30 (m, 2H), 1.97-1.68 (m, 6H).

EXAMPLE 263

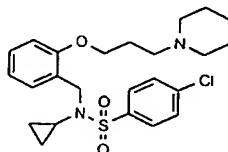
4-bromo-N-(2,5-difluorophenyl)-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride



15 ¹H NMR (300 MHz, CD₃OD) δ (ppm): 7.79 (d, 2H), 7.63 (d, 2H), 7.19 (t, 1H), 7.00 (m, 2H),
20 6.90 (d, 1H), 6.85 (d, 1H), 6.73 (m, 1H), 6.65 (m, 1H), 4.83 (s, 2H), 4.15 (m, 2H), 3.68 (d, 2H), 3.60 (m, 2H), 3.30 (m, 2H), 3.06 (m, 2H), 2.35 (m, 2H), 1.99 (m, 2H), 1.85 (m, 3H), 1.55 (m, 1H).

EXAMPLE 264

4-chloro-N-cyclopropyl-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride

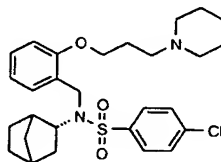


5 $R_f = 0.32$ (10% methanol/DCM) ^1H NMR (500 MHz, CD_3OD) δ (ppm): 7.88-7.86 (d, 2H), 7.67-7.65 (d, 2H), 7.31-7.22 (m, 2H), 6.96-6.88 (dt, 2H), 4.38 (s, 2H), 4.11 (s, 2H), 3.31 (s, 1H), 2.0 (m, 4H), 2.27-2.22 (m, 2H), 1.87-1.78 (m, 6H), 1.66 (m, 2H), 0.47 (m, 4H). ^{13}C NMR (125 MHz, CD_3OD) δ (ppm): 158.4, 140.6, 137.5, 133.0, 130.8, 130.8, 130.7, 125.5, 121.7, 112.4, 66.2, 56.3, 54.8, 52.2, 31.86, 25.7, 24.7, 23.2.

10

EXAMPLE 265

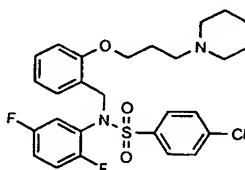
N-[(2S)-bicyclo[2.2.1]hept-2-yl]-4-chloro-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride



15 $R_f = 0.52$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.81 (m, 2H), 7.56 (m, 2H), 7.39 (d, 1H), 7.19 (m, 1H), 6.91 (m, 2H), 4.46 (s, 2H), 4.02 (t, 2H), 3.85 (m, 2H), 2.55 (m, 7H), 2.01 (m, 3H), 1.68-0.99 (m, 14H). ESI calculated for $\text{C}_{28}\text{H}_{31}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 517; Observed: 517.

EXAMPLE 266

4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride



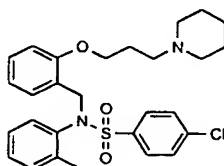
20

$R_f = 0.38$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.69-7.58 (m, 4H), 7.18-6.61 (m, 7H), 4.79 (s, 2H), 4.12 (t, 2H), 3.68-3.56 (m, 4H), 3.07-2.99 (m, 2H), 2.33 (m, 2H), 1.98-1.52 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.6, 141.0, 138.3, 132.9, 131.5, 130.8, 130.5,

127.5, 127.5, 123.4, 121.6, 120.0, 119.7, 118.6, 118.5, 118.4, 118.3, 118.2, 118.1, 112.3, 66.0, 56.3, 54.7, 51.2, 51.1, 25.5, 24.5, 22.9.

EXAMPLE 267

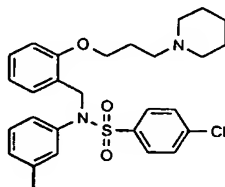
**4-chloro-N-(2-methylphenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide
hydrochloride**



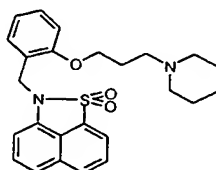
$R_f = 0.59$ (15% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.74-7.65 (m, 4H), 7.24-6.93 (m, 5H), 6.60-6.55 (dd, 3H), 5.47 (d, 1H), 4.14 (m, 4H), 3.80-3.43 (m, 6H), 3.34 (m, 2H), 1.90-1.72 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.7, 141.9, 140.7, 138.5, 138.3, 133.5, 132.1, 131.1, 130.8, 130.61, 129.6, 128.9, 127.3, 123.6, 121.3, 111.9, 65.8, 56.2, 54.6, 52.5, 25.5, 24.5, 22.9, 18.5. ESI calculated for $\text{C}_{28}\text{H}_{33}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 513; Observed: 513.

EXAMPLE 268

**4-chloro-N-(3-methylphenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide
hydrochloride**



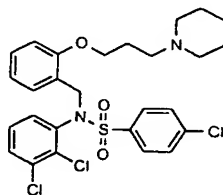
$R_f = 0.32$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.71-7.49 (m, 4H), 7.20-6.94 (m, 4H), 6.84 (d, 1H), 6.69 (m, 3H), 4.80 (s, 2H), 4.04 (t, 2H), 3.22 (m, 2H), 3.06 (b, 4H), 2.29-2.17 (m, 5H), 1.80 (m, 4H), 1.61 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 156.5, 138.5, 138.1, 137.8, 136.4, 130.7, 129.1, 128.8, 128.7, 128.6, 128.0, 127.8, 125.2, 122.7, 119.5, 110.4, 64.6, 54.7, 53.0, 49.3, 24.2, 23.2, 21.8, 19.4. ESI calculated for $\text{C}_{28}\text{H}_{33}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 513; Observed: 513.

EXAMPLE 269**2-{2-[3-(1-piperidinyl)propoxy]benzyl}-2H-naphtho[1,8-cd]isothiazole 1,1-dioxide hydrochloride**

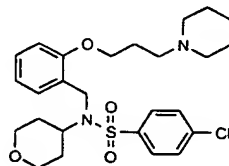
5 $R_f = 0.48$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 8.11-7.97 (dd, 2H), 7.76 (m, 1H), 7.44-7.23 (m, 4H), 6.98 (d, 1H), 6.87 (t, 1H), 6.68 (m, 1H), 4.95 (s, 2H), 4.10 (t, 2H), 2.60-2.41 (m, 6H), 2.02 (m, 2H), 1.57-1.40 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 160.1, 140.2, 134.8, 134.4, 134.0, 133.0, 132.8, 132.7, 131.8, 126.8, 124.1, 123.1, 121.8, 114.7, 107.4, 69.1, 58.9, 57.2, 44.2, 28.6, 27.6, 26.2. ESI calculated for $\text{C}_{25}\text{H}_{28}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 437; Observed: 437.

EXAMPLE 270

10 **4-chloro-N-(2,3-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**

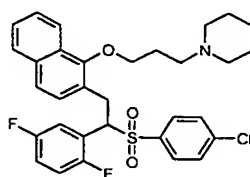


15 $R_f = 0.38$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.73-7.62 (m, 4H), 7.42 (dd, 1H), 7.22-7.10 (m, 2H) 6.85 (d, 1H) 6.83 (dd, 1H), 6.73 (dd, 1H) 6.63 (t, 1H) 5.16 (d, 1H) 4.58 (d, 1H) 4.18 (m, 1H) 4.05 (d, 1H) 3.53-3.30 (m, 6H) 2.36-1.90 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 159.39 141.58, 139.54, 139.42, 136.60, 135.47, 133.69, 132.59, 132.31, 132.15, 131.48, 131.38, 129.32, 123.92, 122.10, 112.87, 66.59, 56.95, 55.31, 51.84, 26.10, 25.07, 23.59. ESI calculated for $\text{C}_{27}\text{H}_{29}\text{Cl}_3\text{N}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 567; Observed: 567.

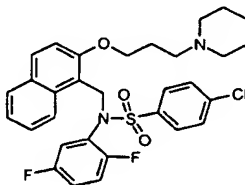
EXAMPLE 271**4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}-N-tetrahydro-2H-pyran-4-ylbenzenesulfonamide hydrochloride**

5 $R_f = 0.42$ (10% methanol/DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.90-7.86 (m, 2H), 7.63-7.69 (m, 2H), 7.41-7.39 (m, 1H), 7.33-7.27 (m, 1H), 6.97-6.92 (m, 2H), 4.56 (s, 2H), 4.16-4.12 (t, 2H), 3.93-3.87 (m, 1H), 3.80-3.73 (m, 2H), 3.44-3.22 (m, 8H), 2.32-2.27 (m, 2H), 1.89-1.80 (m, 4H), 1.61-1.53 (m, 4H), 1.29-1.25 (m, 2H). ^{13}C NMR (free base, 75 MHz, CDCl_3) δ (ppm): 155.1, 139.5, 138.4, 128.9, 128.6, 127.9, 125.6, 120.0, 110.2, 55.7, 55.1, 54.2, 41.0, 30.8, 26.4, 25.4, 23.9, 14.0.

10

EXAMPLE 272**4-chloro-N-(2,5-difluorophenyl)-N-({1-[3-(1-piperidinyl)propoxy]-2-naphthyl}methyl)benzenesulfonamide hydrochloride**

15 $R_f = 0.6$ (10:1 DCM:methanol), ^1H NMR (CD_3OP) δ (ppm): 7.99-7.96 (m, 1H), 7.82-7.76 (m, 3H), 7.66-7.63 (m, 1H), 7.54-7.45 (m, 3H), 7.30-7.28 (m, 1H), 7.05-7.00 (m, 2H), 6.84-6.81 (m, 1H), 5.01-4.91 (m, 2H), 4.04-4.01 (m, 2H), 3.32-3.00 (m, 6H), 2.23-2.26 (m, 2H), 1.81-1.64 (m, 6H). LC-MS calculated for $\text{C}_{31}\text{H}_{31}\text{ClF}_2\text{N}_2\text{O}_3\text{S}$: 585; observed 585.

EXAMPLE 273**4-chloro-N-(2,5-difluorophenyl)-N-({1-[3-(1-piperidinyl)propoxy]-2-naphthyl}methyl)benzenesulfonamide hydrochloride**

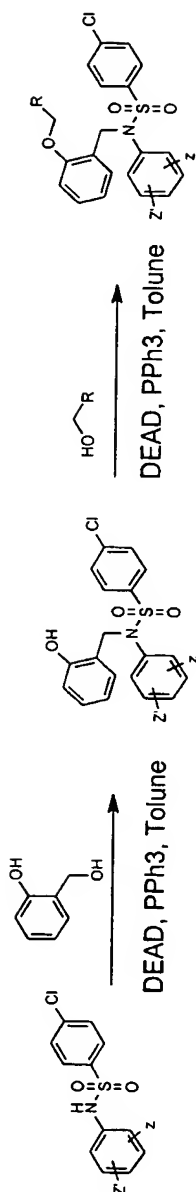
20 $\text{Mp} = 228^\circ\text{C}$ (d). $R_f = 0.45$ (10:1; DCM:methanol). ^1H NMR (DMSO) δ (ppm): 8.20-8.17 (m, 1H), 7.87-7.77 (m, 6H), 7.55-7.11 (m, 5H), 6.57 (m, 1H), 5.25 (m, 2H), 3.95 (m, 2H), 3.40-3.36 (m,

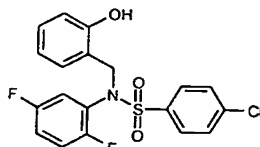
2H), 3.15 (m, 2H), 2.85 (m, 2H), 2.12 (m, 2H), 1.80-1.76 (m, 4H), 1.42 (m, 2H). LC-MS calculated for $C_{31}H_{31}ClF_2N_2O_3S$: 585; observed 585.

EXAMPLE 274

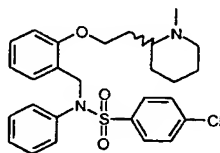
- 5 Using the general synthetic scheme outlined in SCHEME 274, compounds described in Examples 275-283 were prepared.

155

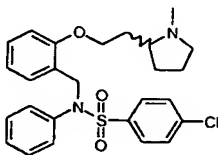
SCHEME 274

EXAMPLE 275**4-chloro-N-(2,5-difluorophenyl)-N-(2-hydroxybenzyl)benzenesulfonamide**

5 $R_f = 0.50$ (3:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.74-7.71 (d, 2H, 7.54-7.51 (d, 2H), 7.20-6.96 (m, 1H), 7.00-6.96 (m, 2H), 6.89-6.87 (m, 2H), 6.75-6.67 (m, 2H), 6.45(s, 1H), 4.70 (s, 2H).

EXAMPLE 276**4-chloro-N-{2-[2-(1-methyl-2-piperidinyl)ethoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride**

10 $R_f = 0.23$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.66-7.60 (m, 4H), 7.22-7.15 (m, 4H), 6.95-6.89 (m, 4H), 6.68 (t, 1H), 5.04 (d, 1H), 4.71 (d, 1H), 4.16 (m, 2H), 3.85 (m, 1H), 3.47 (d, 1H), 3.19 (m, 1H), 2.98 (s, 3H), 2.65 (m, 1H), 2.22 (m, 1H), 2.01-1.64 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.7, 140.9, 140.0, 138.4, 133.3, 131.2, 131.0, 130.9, 130.7, 130.3, 130.0, 124.7, 121.9, 112.7, 64.9, 63.4, 57.4, 51.8, 41.1, 31.5, 28.9, 24.5, 23.1. ESI calculated for $\text{C}_{27}\text{H}_{33}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 499; Observed: 499.

EXAMPLE 277**4-chloro-N-{2-[2-(1-methyl-2-pyrrolidinyl)ethoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride**

20 $R_f = 0.24$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.62 (m, 4H), 7.22-7.16 (m, 4H), 6.96-6.89 (m, 4H), 6.68 (t, 1H), 4.51 (d, 1H), 4.77 (d, 1H), 4.28 (m, 2H), 4.14-4.02 (m, 2H), 3.73 (m, 1H), 3.22 (m, 1H), 3.04 (s, 3H), 2.69-2.44 (m, 2H), 2.28-1.91 (m, 4H). ^{13}C NMR (75

WO 00/50391

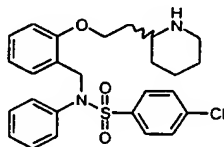
157

PCT/US00/04560

MHz, CD₃OD) δ (ppm): 158.6, 140.8, 139.9, 138.4, 133.4 131.2, 130.9, 130.9 130.7, 130.3, 129.7
124.7, 121.9, 112.7, 67.8, 65.9, 57.8, 51.8, 40.1 31.6 30.5, 22.7.

EXAMPLE 278

4-chloro-N-phenyl-N-{2-[2-(2-piperidinyl)ethoxy]benzyl}benzenesulfonamide hydrochloride



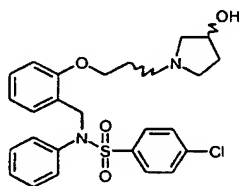
5

$R_f = 0.40$ (14% methanol/DCM) ¹H NMR (300 MHz, CD₃OD) δ (ppm): 7.59-7.52 (m, 4H), 7.15-7.08 (m, 4H), 6.88-6.80 (m, 4H), 6.60 (t, 1H), 4.93 (d, 1H), 4.68 (d, 1H) 4.15-4.05 (m, 2H), 3.79 (m, 1H), 3.37 (m, 1H), 3.10 (m, 1H), 2.26-1.49 (m, 8H). ¹³C NMR (75 MHz, CD₃OD) δ (ppm): 158.6, 140.8, 140.1, 138.5, 133.1, 131.1, 131.0, 130.9, 130.7, 130.4, 129.7, 124.9, 121.9, 112.9, 64.9, 55.9, 51.8, 46.6, 34.9, 29.9, 23.9, 23.5. ESI calculated for C₂₆H₂₉ClN₂O₃S [MH⁺] 485; Observed: 485.

10

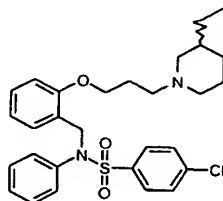
EXAMPLE 279

N-{2-[3-(3-hydroxy-1-pyrrolidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride



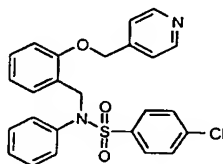
$R_f = 0.15$ (9% methanol/DCM) ¹H NMR (300 MHz, CD₃OD) δ (ppm): 7.52-7.46 (m, 4H), 7.10-7.01 (m, 4H), 6.80-6.73 (m, 4H), 6.54 (m, 1H), 4.74 (s, 2H), 4.48-4.46 (m, 1H), 4.02 (t, 2H), 3.58 (m, 3H), 3.39 (m, 3H), 2.28-1.93 (m, 4H). ¹³C NMR (75 MHz, CD₃OD) δ (ppm): 160.3, 142.4, 141.6, 140.1, 134.8, 132.8, 132.5, 132.4, 131.9, 131.3, 126.4, 123.4, 114.3, 72.4, 67.9, 64.9, 56.9, 55.9, 53.5, 36.0, 29.2. ESI calculated for C₂₇H₂₉ClN₂O₄S [MH⁺] 501; Observed: 501.

15

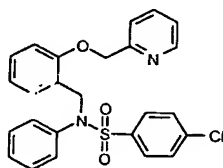
EXAMPLE 280**4-chloro-N-{2-[3-(2-ethyl-1-piperidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride**

5 $R_f = 0.23$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.44-7.59 (m, 4H), 7.24-7.15 (m, 4H), 6.94-6.89 (m, 4H), 6.68 (t, 1H), 4.88 (d, 2H), 4.17 (t, 2H), 3.66-3.52 (d, 3H), 3.25 (m, 2H), 2.33 (m, 2H), 2.03-1.63 (m, 8H), 1.05 (t, 3H), ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.9, 141.0, 140.2, 138.9, 133.4, 131.3, 131.1, 131.0, 130.5, 129.8, 125.0, 122.1, 113.0, 66.9, 65.6, 52.0, 51.9, 51.7, 28.2, 25.8, 24.2, 22.4, 10.8. ESI calculated for $\text{C}_{29}\text{H}_{35}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 527; Observed: 527.

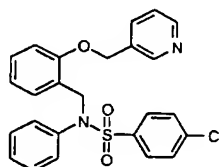
10

EXAMPLE 281**4-chloro-N-phenyl-N-[2-(4-pyridinylmethoxy)benzyl]benzenesulfonamide hydrochloride**

15 $R_f = 0.63$ (5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 8.31 (d, 2H), 7.47-7.38 (m, 4H), 7.25 (d, 2H), 7.11 (m, 1H), 7.02-6.97 (m, 4H), 6.79 (m, 2H), 6.70 (m, 2H), 4.90 (s, 2H), 4.77 (s, 2H).

EXAMPLE 282**4-chloro-N-phenyl-N-[2-(2-pyridinylmethoxy)benzyl]benzenesulfonamide hydrochloride**

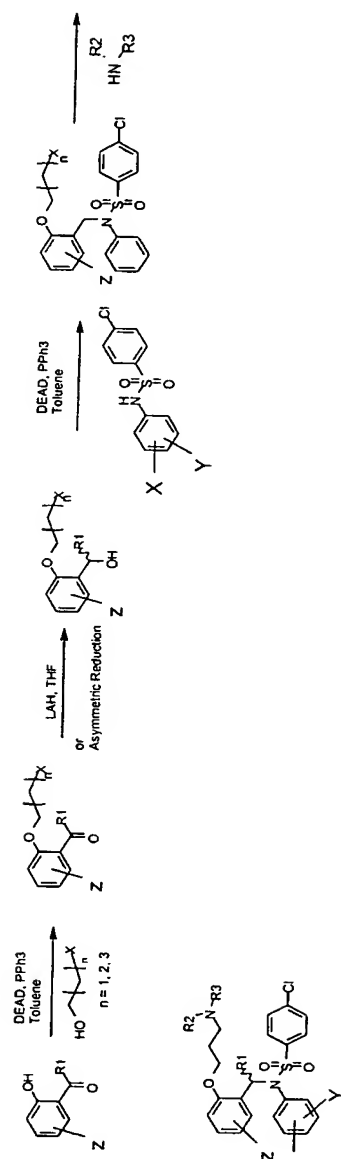
20 $R_f = 0.57$ (5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 8.87 (d, 1H), 9.60 (t, 1H), 8.17 (d, 1H), 8.02 (t, 1H), 7.61 (q, 4H), 7.29-6.86 (m, 9H), 5.47 (s, 2H), 5.00 (s, 2H), ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 156.2, 153.8, 147.5, 143.6, 140.5, 138.3, 136.9, 134.1, 130.6, 130.5, 130.4, 130.0, 129.3, 127.4, 126.8, 125.7, 123.1, 113.5, 68.7, 51.3. ESI calculated for $\text{C}_{25}\text{H}_{21}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 465; Observed: 465.

EXAMPLE 283**4-chloro-N-phenyl-N-[2-(3-pyridinylmethoxy)benzyl]benzenesulfonamide hydrochloride**

$R_f = 0.61$ (5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 8.58-8.51 (m, 2H),
5 7.89, (d, 1H), 7.62-7.44 (m, 5H), 7.30 (dd, 1H), 7.20-7.16 (m, 4H), 6.98-6.84 (m, 4H), 5.07 (s, 2H),
4.90 (s, 2H).

EXAMPLE 284

The general synthetic scheme set forth in SCHEME 284 can also be used for the preparation of numerous compounds according to the invention.

SCHEME 284

2-[(ω -bromo alkyloxy) N-benzyl]4-chlorobenzenesulfanilides

To a stirred suspension of lithium aluminum hydride (1.78 g, 46.8 mmol) in THF (90 mL) at 0 °C was added a solution of salicylanilide (5.0g, 23.4 mmol) in THF (50 mL) over 0.5 h. The resulting mixture was heated at refluxing for 3 h, then cooled to 0 °C, quenched with saturated NaHSO₄ solution, filtered through celite pad and the celite pad was washed with ethyl acetate. The filtrate was diluted with ethyl acetate (300 mL), washed with saturated brine (2 x 100 mL), dried with MgSO₄, filtered and concentrated under reduced pressure to give 3.9 g of the desired product as white solid (y: 83%) R_f = 0.40 (25% ethyl acetate/hexanes) ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.28-7.15 (m, 4H), 7.95- 6.84 (m, 5H), 4.41 (s, 2H).

Sulfonylation of the amine (2.0 g, 10.0 mmol) according to the general procedure described elsewhere provided the desired product (3.40 g, 9.10 mmol, 91%). R_f = 0.35 (25% ethyl acetate/hexanes) ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.66-7.49 (m, 4H), 7.28-7.14 (m 4H), 6.97-6.65 (m, 5H). 4.71 (s, 2H).

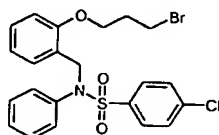
General procedure for alkylation of phenol with ω -bromoalkanols

Mitsunobu alkylation of phenol with 3-bromo propanol, 4-bromo butanol and 5-bromo pentanol according general procedure described elsewhere gave the corresponding 2-[(ω -bromo alkyloxy) N-benzyl]4-chlorobenzenesulfanilides.

General procedure for the amination of 2-[(ω -bromo alkyloxy) N-benzyl]4-chlorobenzenesulfanilides.

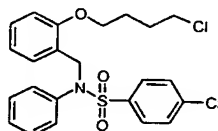
The bromo compound (1.0 eq) was dissolved in neat amine (5.0 eq) (or in DCM (2.0 mL/mmol) if the amine is a solid), and the solution was allowed stir at room temperature under Ar for 1h. The reaction mixture was then concentrated under reduced pressure, re-dissolved in ethyl acetate (25 mL/mmol) washed the ethyl acetate solution with saturated bicarbonate solution and water, dried with MgSO₄, filtered and concentrated under reduced pressure to give the desired product, as the free base, in near quantitative yield. The free base was converted into the corresponding HCl salt as described elsewhere. The HCl salt was purified by passing through a short plug of SiO₂ (10% methanol/DCM) to yield the desired product in >90% yield.

The compounds described in Examples 285-320 were prepared according to the scheme described in the previous example.

EXAMPLE 285**N-[2-(3-bromopropoxy)benzyl]-4-chloro-N-phenylbenzenesulfonamide**

5

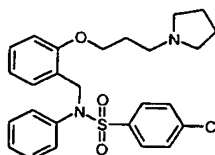
$R_f = 0.35$ (20% ethyl acetate/hexanes) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.55-7.47 (m, 2H), 7.19-7.17 (m, 4H), 7.27-7.14 (m, 5H), 6.98 (m, 2H), 6.86-6.75 (m, 2H), 4.78 (s, 2H), 3.99 (t, 2H), 3.53 (t, 2H), 2.20 (q, 2H).

EXAMPLE 286**4-chloro-N-{2-[(5-chloropentyl)oxy]benzyl}-N-phenylbenzenesulfonamide**

10

$R_f = 0.17$ (6% ethyl acetate/hexanes) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.59-6.70 (m, 13H), 3.82 (t, 2H), 3.56 (t, 2H), 1.83-1.54 (m, 6H).

15

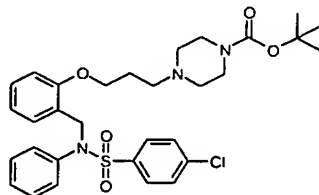
EXAMPLE 287**4-chloro-N-phenyl-N-{2-[3-(1-pyrrolidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**

$R_f = 0.60$ (6:1:DCM:methanol). ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.55-7.47 (m, 4H), 7.19-7.17 (m, 3H), 6.79-6.75 (m, 3H), 6.61 (d, 2H), 4.75 (s, 2H), 4.13 (br, 2H), 3.80-3.65 (m, 4H), 3.15 (br, 2H), 2.60 (br, 2H), 2.15 (m, 4H).

20

EXAMPLE 288

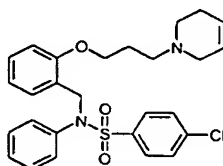
tert-butyl 4-{3-[2-({[(4-chlorophenyl)sulfonyl]anilino}methyl)phenoxy]propyl}-1-piperazinecarboxylate



5 $R_f = 0.13$ (5% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.56 (m, 2H), 7.45 (m, 2H), 7.32-7.12 (m, 5H), 6.99 (m, 2H), 6.83 (t, 1H), 6.73 (d, 1H), 5.30 (s, 2H), 3.89 (t, 2H), 3.44 (t, 4H), 2.50-2.37 (m, 6H), 1.87 (q, 2H), 1.47 (s, 9H).

EXAMPLE 289

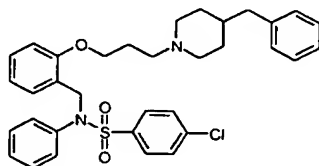
4-chloro-N-{2-[3-(3,6-dihydro-1(2H)-pyridinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride



10 $R_f = 0.45$ (5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.40 (m, 4H), 6.95 (m, 4H), 6.71-6.60 (m, 4H), 6.43 (m, 1H), 5.82 (m, 1H), 5.59 (m, 1H), 4.65 (s, 2H), 3.97 (t, 2H), 3.71 (m, 2H), 3.55-3.10 (m, 4H), 2.33-1.81 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.8, 140.9, 139.9, 138.5, 133.4, 131.2, 130.9, 130.8, 130.3, 129.6, 127.1, 124.7, 121.8, 121.4, 112.6, 66.3, 55.7, 52.0, 52.0, 51.0, 25.9, 24.1.

EXAMPLE 290

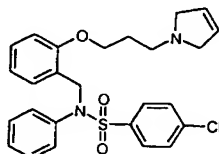
N-{2-[3-(4-benzyl-1-piperidiny)propoxy]benzyl}-4-chloro-N-phenylbenzenesulfonamide hydrochloride



20 $R_f = 0.60$ (14% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.54 (m, 4H), 7.21-7.06 (m, 9H), 6.82-6.74 (m, 4H), 6.57 (m, 1H), 4.78 (s, 2H), 4.07 (m, 2H), 3.55 (m, 4H), 2.99 (m, 2H), 2.58 (m, 2H), 2.27 (m, 2H), 1.89-1.51 (m, 5H).

EXAMPLE 291

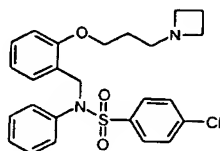
N-{2-[3-(4-benzyl-1-piperidiny)propoxy]benzyl}-4-chloro-N-phenylbenzenesulfonamide hydrochloride



5 $R_f = 0.32$ (9% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.40 (m, 4H), 6.99 (m, 4H), 6.69-6.44 (m, 5H), 5.80 (s, 2H), 4.66 (s, 2H), 4.07-3.96 (m, 6H), 3.62 (m, 2H), 2.11 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 161.0, 143.0, 142.0, 140.6, 135.6, 133.4, 133.0, 132.9, 132.4, 131.8, 128.7, 126.8, 123.9, 114.7, 68.2, 63.7, 56.9, 54.2, 29.6.

EXAMPLE 292

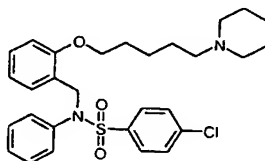
10 **N-{2-[3-(1-azetidiny)propoxy]benzyl}-4-chloro-N-phenylbenzenesulfonamide hydrochloride**



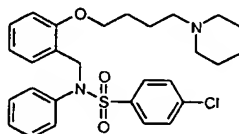
15 $R_f = 0.54$ (14% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.61-7.54 (m, 4H), 7.16-7.09 (m, 4H), 6.88-6.78 (m, 4H), 6.60 (t, 1H), 4.84 (s, H), 4.25 (t, 4H), 4.08 (m, 2H), 3.67 (m, 2H), 2.52 (m, 2H), 2.10 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.8, 140.9, 139.9, 138.4, 133.4, 131.2, 130.9, 130.77, 130.3, 129.6, 124.6, 121.8, 112.6, 65.8, 56.2, 54.1, 52.0, 26.2, 17.6.

EXAMPLE 293

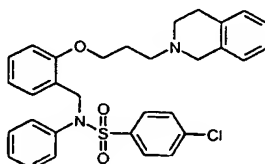
4-chloro-N-phenyl-N-(2-{[5-(1-piperidiny)pentyl]oxy}benzyl)benzenesulfonamide hydrochloride



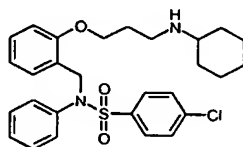
20 $R_f = 0.17$ (20% methanol/ethyl acetate) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.89-7.82 (m, 4H), 7.47-7.36 (m, 4H), 7.27-7.09 (m, 4H), 6.96-6.91 (m, 1H), 5.09 (s, 2H), 4.23 (t, 2H), 3.81 (d, 2H), 3.42 (t, 2H), 3.20 (m, 2H), 2.25-1.95 (m, 12H).

EXAMPLE 294**4-chloro-N-phenyl-N-{2-[4-(1-piperidinyl)butoxy]benzyl}benzenesulfonamide hydrochloride**

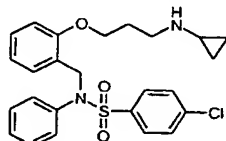
$R_f = 0.20$ (5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.38 (m, 4H), 6.97 (m, 4H), 6.69 (m, 4H), 6.44 (t, 1H), 4.64 (s, 2H), 3.84 (t, 2H), 2.99 (m, 6H), 1.93-1.68 (m, 10H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.5, 140.3, 139.8, 138.3, 132.5, 130.5, 130.4, 130.4, 130.3, 129.8, 129.0, 124.5, 121.1, 112.3, 68.1, 58.1, 54.3, 51.3, 27.6, 25.3, 22.7, 22.3. ESI calculated for $\text{C}_{28}\text{H}_{33}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 511; Observed: 511.

EXAMPLE 295**4-chloro-N-{2-[3-(3,4-dihydro-2(1H)-isoquinolinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide**

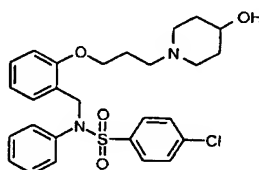
$R_f = 0.50$ (50% ethyl acetate/hexanes) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.59-7.55 (m, 2H), 7.46-7.42 (m, 2H), 7.44 (dd, 1H), 7.22-6.99 (m, 10H), 6.84 (t, 1H), 6.74 (t, 1H), 3.92 (t, 2H), 3.62 (s, 2H), 2.91 (t, 2H), 2.73 (t, 2H), 2.62 (t, 2H), 1.96 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 159.1, 141.7, 141.6, 139.7, 137.2, 136.8, 132.6, 131.6, 131.4, 131.3, 131.2, 130.4, 129.1, 128.7, 128.2, 126.4, 122.9, 113.6, 68.6, 58.7, 57.4, 53.5, 51.8, 31.7, 29.5. ESI calculated for $\text{C}_{31}\text{H}_{31}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 547; Observed: 547.

EXAMPLE 296**4-chloro-N-{2-[3-(cyclohexylamino)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride**

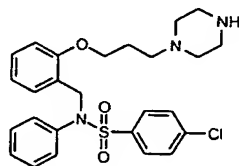
$R_f = 0.20$ (14% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.45-7.37 (m, 4H), 7.45-7.11 (m, 4H), 7.-7.11 (m, 4H), 6.89 (m, 1H), 5.09 (s, 2H), 4.38 (t, 2H), 3.72 (t, 2H), 3.40 (m, 1H), 2.49 (m, 4H), 2.13-1.94 (m, 3H), 1.66-1.48 (m, 5H). ^{13}C NMR (75 MHz, CD_3OD) δ 158.6, 140.7, 140.1, 138.6, 133.0, 131.07, 130.9, 130.9, 130.7, 130.3, 129.6, 124.9, 121.8, 112.8, 66.5, 59.1, 51.6, 44.1, 30.9, 28.1, 26.6, 25.9. ESI calculated for $\text{C}_{28}\text{H}_{33}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 513; Observed: 513.

EXAMPLE 297**4-chloro-N-{2-[3-(cyclopropylamino)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride**

5 $R_f = 0.32$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.40-7.32 (m, 4H), 6.99-6.89 (m, 5H), 6.76-6.74 (m, 2H), 6.57 (m, 2H), 4.61 (s, 2H), 3.71 (t, 2H), 2.66 (t, 2H), 1.99 (m, 1H), 1.71 (m, 2H), 0.30-0.15 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 159.0, 141.1, 139.3, 132.6, 131.3, 131.2, 131.1, 130.7, 129.8, 125.8, 122.2, 113.2, 68.1, 51.2, 48.4, 32.6, 30.8, 6.8. ESI calculated for $\text{C}_{25}\text{H}_{27}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 471; Observed: 471.

EXAMPLE 298**4-chloro-N-{2-[3-(4-hydroxy-1-piperidiny)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride**

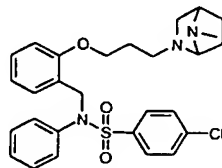
10 $R_f = 0.19$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.50-7.43 (m, 4H), 7.07-6.98 (m, 4H), 6.78-6.72 (m, 4H), 6.54-6.49 (m, 1H), 4.17 (s, 2H), 3.98 (t, 2H), 3.81 (m, 1H), 3.39-3.08 (m, 6H), 2.20-2.11 (m, 2H), 1.98-1.91 (m, 2H), 1.70 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.7, 140.8, 140.1, 138.6, 133.2, 131.2, 130.9, 130.9, 130.8, 130.3, 129.6, 124.8, 121.8, 112.7, 66.6, 56.3, 51.8, 51.3, 32.6, 26.2. ESI calculated for $\text{C}_{27}\text{H}_{31}\text{ClN}_2\text{O}_4\text{S}$ $[\text{MH}^+]$ 515; Observed: 515.

EXAMPLE 299**4-chloro-N-phenyl-N-{2-[3-(1-piperaziny)propoxy]benzyl}benzenesulfonamide dihydrochloride**

20 $R_f = 0.15$ (14% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.80-7.65 (m, 5H), 7.33-7.27 (m, 4H), 7.07-6.91 (m, 4H), 6.77 (t, 1H), 5.01 (s, 2H), 4.34 (t, 2H), 4.02-3.68 (m, 10H), 2.59 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.7, 140.8, 139.8, 138.5, 13.3, 133.1, 131.2, 130.9, 130.9, 130.8, 130.3, 129.7, 124.7, 121.8, 112.7, 66.1, 56.5, 52.0, 50.3, 50.3, 42.4, 25.6. ESI calculated for $\text{C}_{26}\text{H}_{30}\text{ClN}_3\text{O}_3\text{SCl}$ $[\text{MH}^+]$ 500; Observed: 500.

EXAMPLE 300

4-chloro-N-(2-[(2S)-7-methyl-7-azabicyclo[2.2.1]hept-2-yl]methoxy)benzyl)-N-phenylbenzenesulfonamide hydrochloride

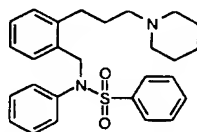


5 $R_f = 0.20$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.65-7.59 (m, 4H), 7.25-7.16 (m, 4H), 7.00-6.93 (m, 4H), 6.73 (m, 1H), 4.88 (q, 2H), 4.10 (m, 1H), 3.97 (m, 3H), 2.76 (s, 3H), 2.54 (m, 1H), 2.23-1.78 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.7, 140.8, 140.3, 138.7, 133.0, 131.1, 130.9, 130.8, 130.7, 130.3, 129.6, 125.2, 122.0, 113.2, 70.5, 68.1, 66.1, 51.7, 43.3, 34.4, 33.8, 3.1, 25.8. ESI calculated for $\text{C}_{27}\text{H}_{29}\text{N}_2\text{O}_3\text{SCl}$ $[\text{MH}^+]$ 497; Observed: 497.

10

EXAMPLE 301

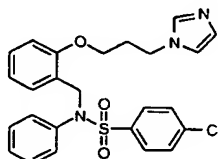
N-phenyl-N-{2-[4-(1-piperidiny)butyl]benzyl}benzenesulfonamide



15 $R_f = 0.33$ (5% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.67-7.62 (m, 2H), 7.55-7.50 (m, 2H), 7.21-7.11 (m, 5H), 6.94-6.83 (m, 4H), 4.75 (s, 2H), 2.99-2.80 (m, 8H), 2.05-1.62 (m, 10H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 141.5, 138.5, 137.9, 133.4, 132.6, 131.4, 130.0, 129.4, 129.2, 129.2, 128.7, 128.5, 128.1, 126.2, 57.9, 53.7, 53.0, 31.9, 29.1, 24.5, 23.5, 22.9.

EXAMPLE 302

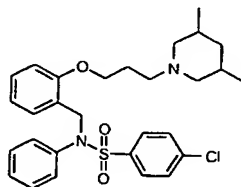
4-chloro-N-(2-[3-(1H-imidazol-1-yl)propoxy]benzyl)-N-phenylbenzenesulfonamide hydrochloride



20 $R_f = 0.38$ (10% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.53-7.38 (m, 5H), 7.04-6.93 (m, 5H), 6.85-6.75 (m, 4H), 6.55 (m, 1H), 6.50 (t, 1H), 4.70 (s, 2H), 4.18 (t, 2H), 3.72 (t, 2H), 2.06 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 157.6, 139.6, 139.4, 137.7, 131.9, 129.9, 129.8, 129.7, 129.6, 129.2, 128.5, 124.0, 120.6, 111.4, 64.7, 50.5, 44.4, 31.3. ESI calculated for $\text{C}_{25}\text{H}_{29}\text{ClN}_3\text{O}_3\text{S}$ $[\text{MH}^+]$ 482; Observed: 482.

EXAMPLE 303

4-chloro-N-{2-[3-(3,5-dimethyl-1-piperidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride

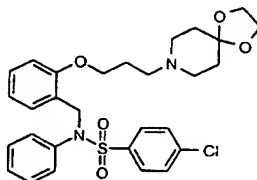


5 $R_f = 0.35$ (9% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.66-7.58 (m, 4H), 7.23-7.14 (m, 4H), 6.99-6.88 (m, 4H), 6.70 (t, 1H), 4.87 (s, 2H), 4.09 (t, 2H), 3.44-2.83 (m, 4H), 2.39-1.85 (m, 6H), 1.11-0.77 (m, 8H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.9, 140.9, 140.3, 138.7, 133.2, 131.2, 131.1, 131.02, 130.9, 130.4, 129.7, 125.0, 121.9, 112.8, 67.0, 66.9, 60.8, 57.5, 56.8, 51.7, 41.7, 38.5, 31.3, 26.4, 26.3, 19.7, 19.3.

10

EXAMPLE 304

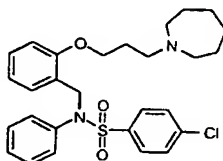
4-chloro-N-{2-[3-(1,4-dioxo-8-azaspiro[4.5]dec-8-yl)propoxy]benzyl}-N-phenylbenzenesulfonamide



15 $R_f = 0.38$ (9% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.58-7.55 (m, 2H), 7.46-7.36 (m, 3 H), 7.23-7.11 (m, 4H), 7.00 (dd, 2H), 6.85 (t, 1H), 6.72 (d, 1H), 4.79 (s, 2H), 3.83 (t, 2H), 2.52-2.44 (m, 6H), 1.90-1.74 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 156.8, 139.6, 139.4, 137.5, 130.4, 129.5, 129.50, 129.2, 128.2, 124.3, 120.8, 111.4, 107.6, 66.7, 64.6, 55.2, 51.8, 49.5, 35.2, 27.4.

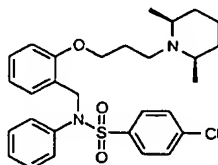
EXAMPLE 305

N-{2-[3-(1-azepanyl)propoxy]benzyl}-4-chloro-N-phenylbenzenesulfonamide hydrochloride

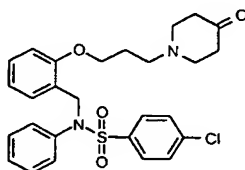


20 $R_f = 0.19$ (9% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.68-7.61 (m, 4H), 7.25-7.16 (m, 4H), 6.97-6.86 (m, 4H), 6.68 (m, 1H), 4.89 (s, 2H), 4.18 (t, 2H), 3.69 (m, 2H), 3.50 (t, H), 2.37 (m, 2H), 2.00 (b, 4H), 1.79 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 161.0, 143.0, 142.2, 140.7, 135.5, 133.4, 133.1, 133.0, 132.5, 131.9, 126.9, 124.0, 114.8, 68.7, 59.3, 58.7, 54.1, 30.2, 28.4, 27.6.

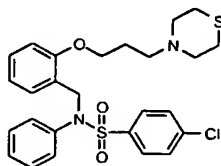
25

EXAMPLE 306**4-chloro-N-(2-{3-[(2R,6S)-2,6-dimethylpiperidinyl]propoxy}benzyl)-N-phenylbenzenesulfonamide hydrochloride**

$R_f = 0.23$ (9% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.44 (m, 4H), 7.06-7.99 (m, 4H), 6.85-6.72 (m, 4H), 6.57 (m, 1H), 4.70 (s, 2H), 3.96 (t, 2H), 3.43-3.23 (m, 6H), 2.11-1.51 (m, 8H), 1.29 (d, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.4, 140.8, 140.3, 138.7, 132.6, 130.9, 130.7, 130.4, 129.6, 125.2, 122.1, 113.1, 66.8, 61.2, 51.1, 24.0, 19.2. ESI calculated for $\text{C}_{29}\text{H}_{35}\text{ClN}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 527; Observed: 527.

EXAMPLE 307**4-chloro-N-{2-[3-(4-oxo-1-piperidiny)]propoxy}benzyl}-N-phenylbenzenesulfonamide hydrochloride**

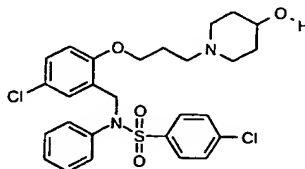
$R_f = 0.25$ (5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.76-7.64 (m, 4H), 7.33-7.18 (m, 5H), 7.06 (dd, 2H), 6.94 (d, 1H), 6.84 (t, 1H), 4.82 (s, 2H), 3.99 (t, 2H), 2.72 (t, 4H), 2.60 (m, 2H), 2.39 (t, 4H), 1.87 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 212.0, 159.4, 141.9, 141.8, 139.9, 139.2, 131.9, 131.8, 131.7, 131.6, 130.7, 126.6, 123.1, 113.8, 68.7, 56.8, 55.9, 52.3, 44.0, 30.0.

EXAMPLE 308**4-chloro-N-phenyl-N-{2-[3-(4-thiomorpholinyl)propoxy]benzyl}benzenesulfonamide hydrochloride**

$R_f = 0.40$ (5% methanol/DCM) ^1H NMR (300 MHz, DMSO) δ (ppm): 7.40 (dd, 4H), 7.04 - 6.88 (m, 4H), 6.77 (m, 2H), 6.57 (dt, 3H), 4.51 (s, 2H), 3.63 (t, 2H), 2.35-2.25 (m, 10H), 1.51 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 156.9, 139.4, 139.4, 137.5, 130.6, 129.4, 129.2, 129.2, 128.2, 124.18, 120.7, 111.3, 66.3, 56.1, 55.4, 49.7, 28.3, 26.6.

EXAMPLE 309

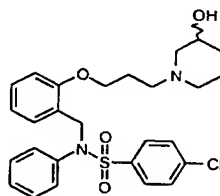
4-chloro-N-{5-chloro-2-[3-(4-hydroxy-1-piperidiny)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride



$R_f = 0.18$ (10:1; DCM:methanol). ^1H NMR (CD_3OD) δ (ppm): 7.44-7.37 (m, 4H), 7.06-7.03 (m, 3H), 6.95 (dd, 1H), 6.76-6.67 (m, 4H), 4.63 (s, 2H), 3.88 (t, 2H), 3.71 (br, 1H), 3.21-3.11 (m, 4H), 2.86 (br, 2H), 2.08-1.99 (m, 2H), 1.89-1.73 (m, 2H), 1.62 (m, 2H).

EXAMPLE 310

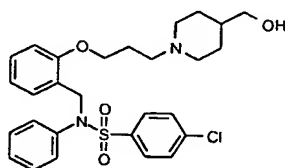
4-chloro-N-{2-[3-(3-hydroxy-1-piperidiny)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride



$R_f = 0.23$ (9% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.66-7.59 (m, 4H), 7.23-7.14 (m, 4H), 7.03-6.87 (m, 4H), 6.72 (t, 1H), 4.87 (s, 2H), 4.06 (t, 2H), 3.94 (b, 1H), 3.21-3.03 (m, 6H), 2.18-1.56 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 157.7, 139.8, 139.2, 137.6, 131.9, 130.0, 129.9, 129.8, 129.7, 129.2, 128.5, 124.0, 120.7, 111.7, 66.0, 65.1, 59.6, 55.9, 53.8, 50.4, 31.4, 25.5, 20.3.

EXAMPLE 311

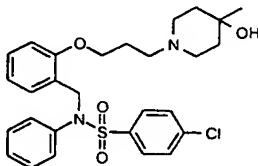
4-chloro-N-(2-{3-[4-(hydroxymethyl)-1-piperidiny]propoxy}benzyl)-N-phenylbenzenesulfonamide hydrochloride



$R_f = 0.20$ (9% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.41-7.34 (m, 4H), 6.99-6.90 (m, 4H), 6.71-6.63 (m, 4H), 6.43 (m, 1H), 4.63 (s, 2H), 3.90 (t, 2H), 3.47-3.24 (m, 6H), 2.82 (m, 2H), 2.09 (m, 2H), 1.81-1.33 (m, 5H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.6, 140.7, 139.8, 138.3, 133.1, 131.0, 130.7, 130.56, 130.1, 129.4, 124.5, 121.6, 112.4, 66.8, 66.3, 56.2, 54.1, 51.6, 37.9, 27.7, 26.0.

EXAMPLE 312

4-chloro-N-{2-[3-(4-hydroxy-4-methyl-1-piperidinyloxy)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride

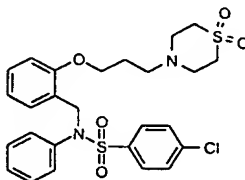


5 $R_f = 0.3$ (1:10; methanol:DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.52-7.45 (m, 4H), 7.09-7.01 (m, 4H), 6.91-6.73 (m, 4H), 6.53 (m, 1H), 4.74 (s, 2H), 4.01 (s, 2H), 3.46-3.22 (m, 6H), 2.19 (m, 2H), 1.84-1.68 (m, 4H), 1.18 (s, 3H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 159.4, 141.4, 140.6, 139.2, 133.9, 131.8, 131.5, 131.5, 131.4, 130.9, 130.3, 125.4, 122.4, 113.3, 67.1, 66.9, 56.7, 52.5, 51.4, 37.6, 30.7, 26.8.

10

EXAMPLE 313

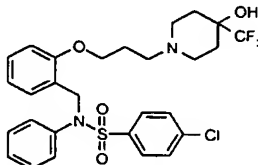
4-chloro-N-{2-[3-(1,1-dioxido-4-thiomorpholinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride



15 $R_f = 0.45$ (67% ethyl acetate/hexanes) ^1H NMR (300 MHz, DMSO) δ (ppm): 7.72-7.60 (m, 4H), 7.30-7.13 (m, 5H), 7.01 (dd, 2H), 6.89 (d, 1H), 6.79 (t, 1H), 4.77 (s, 2H), 3.92 (t, 2H), 3.09 (m, 4H), 2.88 (m, 4H), 2.62 (t, 2H), 1.78 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 155.9, 138.3, 138.1, 136.3, 130.0, 128.4, 128.3, 128.3, 128.2, 128.1, 127.2, 122.8, 119.5, 110.2, 64.7, 52.6, 52.5, 49.9, 49.1. ESI calculated for $\text{C}_{26}\text{H}_{29}\text{ClN}_2\text{S}_2\text{O}_5$ $[\text{MH}^+]$ 549; Observed: 549.

EXAMPLE 314

20 **4-chloro-N-(2-{3-[4-hydroxy-4-(trifluoromethyl)-1-piperidinyloxy]propoxy}benzyl)-N-phenylbenzenesulfonamide hydrochloride**

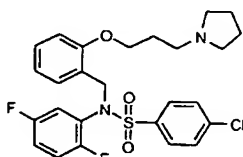


25 $R_f = 0.23$ (5% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.4-7.35 (m, 4H), 7.01-6.91 (m, 5H), 6.78-6.74 (m, 2H), 6.58-6.52 (m, 2H), 4.63 (s, 2H), 3.73 (t, 2H), 2.68 (m, 2H), 2.42 (m, 2H), 2.19 (dt, 2H), 1.79-1.53 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 160.9, 142.9, 141.1,

134.5, 133.1, 133.0, 132.90, 132.8, 132.4, 131.6, 127.6, 123.9, 114.9, 73.9, 73.6, 69.9, 58.9, 53.1, 51.5, 32.9, 30.0. ESI calculated for $C_{28}H_{30}ClF_3N_2O_4S$ $[MH^+]$ 583; Observed: 583.

EXAMPLE 315

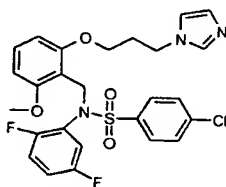
5 **4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-pyrrolidinyloxy)propoxy]benzyl}benzenesulfonamide hydrochloride**



$R_f = 0.40$ (10:1; DCM:methanol). 1H NMR (300 MHz, CD_3OD) δ (ppm): 7.85-7.74 (m, 4H), 7.31 (dt, 1H), 7.16-6.76 (m, 6H), 4.96 (s, 2H), 4.26 (t, 2H), 3.80 (m, 2H), 3.58 (br m, 4H), 2.48-2.39 (m, 2H), 2.57-2.11 (m, 4H).

EXAMPLE 316

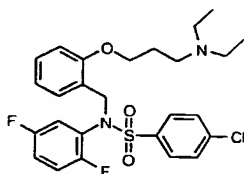
10 **4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1H-imidazol-1-yl)propoxy]-6-methoxybenzyl}benzenesulfonamide hydrochloride**



15 $R_f = 0.5$ (93:7; DCM:methanol). 1H NMR ($CDCl_3$) δ (ppm): 7.77-7.34 (m, 3H), 7.63-7.60 (m, 2H), 7.22-7.19 (m, 1H), 7.12 (t, 1H), 7.00-6.95 (m, 2H), 6.60-6.54 (m, 1H), 6.49-6.46 (m, 1H), 6.37-6.35 (m, 1H), 4.94-4.90 (m, 2H), 4.43 (t, 2H), 3.91 (t, 3H), 3.47 (s, 3H), 2.29 (m, 2H). LC-MS Calculated for $C_{26}H_{24}ClF_2N_3O_4S$: 547. Observed: 548 (MH^+).

EXAMPLE 317

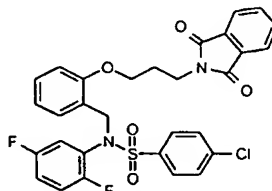
20 **4-chloro-N-{2-[3-(diethylamino)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide hydrochloride**



$R_f = 0.49$ (9 % methanol in DCM), 1H NMR (300 MHz, CD_3OD) δ (ppm): 7.71 (d, 2H), 7.62 (d, 2H), 7.20 (t, 1H), 7.02-6.98 (m, 2H), 6.90 (d, 1H), 6.88 (d, 1H), 6.76 (m, 1H), 6.69 (t, 1H), 4.84 (s, 2H), 4.16 (t, 2H), 3.64-3.61 (m, 2H), 3.37-3.31 (m, 4H), 2.34-2.31 (m, 2H), 1.38 (t, 6H).

EXAMPLE 318

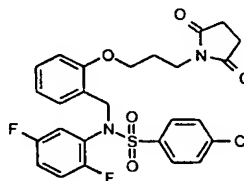
4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propoxy]benzyl}benzenesulfonamide



- 5 $R_f = 0.33$ (2:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.85-7.26 (m, 2H), 7.74-7.67 (m, 4H), 7.48 (d, 2H), 7.31 (d, 1H), 7.17 (t, 1H), 6.94-6.83 (m, 4H), 6.70 (d, 1H), 4.82 (s, 1H), 3.86-3.81 (m, 4H), 2.10-2.01 (m, 2H).

EXAMPLE 319

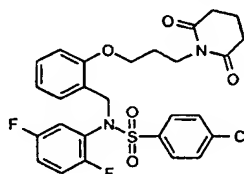
4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(2,5-dioxo-1-pyrrolidinyl)propoxy]benzyl}benzenesulfonamide



- 10 $R_f = 0.73$ (5% methanol in CH_2Cl_2) $^1\text{H NMR}$ (300MHz CDCl_3) δ (ppm): 7.70-7.67 (d, 2H), 7.49-7.46 (d, 2H), 7.31-7.15 (m, 2H), 6.94-6.83 (4H), 6.72-6.69 (d, 1H), 4.89-4.82 (br, 2H), 3.83-3.79 (t, 2H), 3.68-3.63 (t, 2H), 2.77-2.64 (br, 4H), 2.05-1.92 (m, 2H). LC-MS calculated for
15 $\text{C}_{26}\text{H}_{23}\text{ClF}_2\text{N}_2\text{O}_5\text{S}$ $[\text{MH}^+]$ 549; Observed: 549.

EXAMPLE 320

4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(2,6-dioxo-1-piperidiny)propoxy]benzyl}benzenesulfonamide



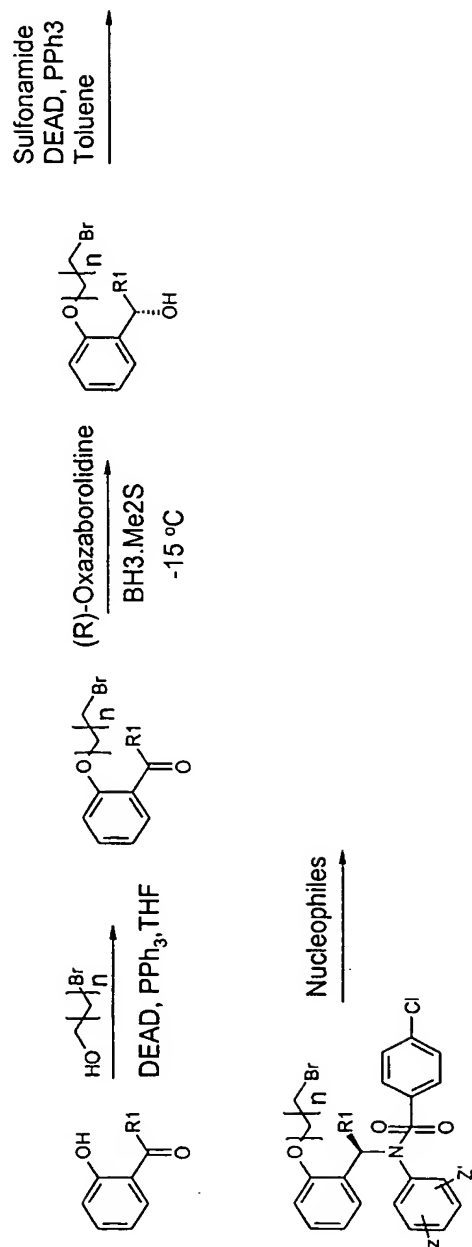
- 20 $R_f = 0.43$ (1:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.68 (d, 2H), 7.48 (d, 2H), 7.36 (d, 1H), 7.17 (m, 1H), 6.94-6.85 (m, 4H), 6.69 (d, 1H), 4.85 (s, 2H), 3.86 (t, 2H), 3.77 (t, 2H), 2.65 (t, 4H), 1.98-1.82 (m, 4H). MS calculated for $\text{C}_{27}\text{H}_{25}\text{ClF}_2\text{N}_2\text{O}_5\text{S}$, $[\text{MH}^+]$ 563; Observed: 563.

EXAMPLE 321

4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride

The general synthetic scheme set forth in SCHEME 321 can also be used for the preparation of
5 numerous compounds according to the invention.

175

SCHEME 321

To a solution of 2'-hydroxy acetophenone (3.0 g, 22 mmol) under Ar, in anhydrous THF (100 mL) was added triphenylphosphine (8.7 g, mm mmol), 3-bromopropanol (3.8 g, 27 mmol) and DEAD (5.2 mL, 33 mmol). The reaction mixture was stirred at room temperature for 14 h, concentrated under reduced pressure and the product isolated by SiO₂ chromatography (hexanes/ethyl acetate 7:1) to give 4.0 g of product (yield: 71%). ¹H NMR (300 MHz, CD₃OD) δ (ppm): 7.72 (dd, 1H), 7.46 (dt, 1H), 7.02-6.95 (m, 2H), 4.22 (t, 2H), 3.61 (t, 2H), 2.60 (s, 3H), 2.38, (p, 2H).

A solution of 2'(3-bromopropoxy) acetophenone (3.2 g, 12.5 mmol) in methanol (50 mL) was cooled to 0 °C under Ar atmosphere. Solid NaBH₄ (0.475 g, 12.5 mmol) was added in one portion and the reaction mixture was stirred at 0° C for 1 h, diluted with 100 mL of water and the product extracted with 3 x 50 mL of ethyl acetate. The combined organic phase was washed with 100 mL of water, dried with anhydrous MgSO₄, filtered and concentrated under reduced pressure to give 3.1 g of product (y: 97%). ¹H NMR (300 MHz, CD₃OD) δ (ppm): 7.38 (dd, 1H), 7.23 (dt, 1H), 6.98 (t, 1H), 6.89 (d, 1H), 5.13 (q, 1H), 4.17 (t, 2H), 3.61 (t, 2H), 2.36 (p, 2H), 1.50 (d, 3H).

15 **Synthesis of *R*-Alcohol**

To a stirred solution of commercially available (Strem)(*R*)- methyl oxazaborolidine (1.27 M solution in toluene, 3.9 mL, 4.95 mmol) at room temperature under Ar was added a solution BH₃.Me₂S (10.5 M, 5.63 mL, 59.1 mmol) over a period of 10 min. The reaction mixture was left stirred at room temperature for 10 min after which time cooled to -20°C. To this cooled solution was added a solution of the ketone (25 33 g, 98.5 mmol) in dry DCM (11 mL) via syringe pump over a period of 4 h. The reaction mixture was left stirred for another 2 h at -20 °C and carefully quenched with pre cooled methanol. The solvent was removed by concentrating under reduced pressure to yield the crude product which was subsequently purified by SiO₂ chromatography(ethyl acetate:hexanes, 1:10) to yield the chiral product as a colorless oil (24 g, 94%, >98% ee by chiral HPLC). The stereochemistry is assigned *S*, based on the literature precedents. ¹H NMR (300 MHz, CD₃OD) δ (ppm): 7.72 (dd, 1H), 7.46 (dt, 1H), 7.02-6.95 (m, 2H), 4.22 (t, 2H), 3.61 (t, 2H), 2.60 (s, 3H), 2.38, (p, 2H).

The procedure was repeated with (*S*)-methyl oxazaborolidine solution to yield the corresponding (*R*)-alcohol.

To a stirred solution of the racemic alcohol (0.5 g, 1.9 mmol) in dry THF (10 mL) under Ar was added triphenylphosphine (0.75g, 2.85 mmol) followed by the sulfonamide (0.91g, 2.85 mmol). The reaction mixture was cooled to 0 °C in an ice bath and DEAD (0.45 mL, 2.85 mmol) was added over period of 5 min. The reaction mixture was left to stir at room temperature for 15h then concentrated under reduced pressure to give the crude product mixture which was subsequently purified by chromatography over SiO₂ (10:1 hexanes/ethyl acetate) to give 465 mg (y: 63%) to a fford a pale

yellow oil. ^1H NMR (500 MHz CDCl_3) δ (ppm): 7.62-7.61(m, 2H), 7.39-7.36 (m, 2H), 7.20 (t, 1H), 6.93 (br, 1H), 6.86 (d overlaps br, 3H), 6.77 (br d, 1H), 6.68 (t, 1H), 6.08 (br, 1H), 4.19-4.09 (m, 2H), 3.77 (br, 2H), 2.47-2.35 (m, 2H), 1.56 (overlapping d, 3H).

The *R* and *S* alcohols were similarly converted to the *S* and *R* bromoalkyl sulfonamide derivative respectively.

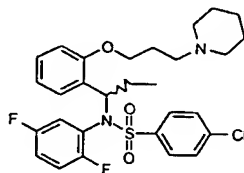
The racemic bromo alkyl sulfonamide derivative (115 mg, 0.21 mmol) was dissolved in dry piperidine (2 mL) under Ar and stirred at room temperature for 1h. The reaction mixture was concentrated under reduced pressure, re-dissolved in 20 mL of ethyl acetate, washed with saturated bicarbonate solution (2x 10 mL of), water (2 x 10 mL), dried with MgSO_4 , filtered and concentrated under reduce pressure to give 110 mg of product as colorless oil (free base). The free base was converted to the HCl salt as described before, passed through a short plug of SiO_2 (10% methanol in DCM) to yield 85 mg of product as white solid. (y: 70%) ^1H NMR (500 MHz CDCl_3) δ (ppm): 7.68-7.54 (m, 4H), 7.23, 7.01, 6.81, 6.67 (br, 6H), 6.25 (q overlaps br, 2H), 4.32-4.21(m, 2H), 3.70-3.60 (m, 4H), 3.10-3.56 (br, 2H), 2.43-2.40 (m, 2H), 2.01-1.75 (m, 5H), 1.55-1.51 (m, 4H). ESI calculated for $\text{C}_{28}\text{H}_{32}\text{ClF}_2\text{N}_2\text{O}_3\text{S}$ [MH+] 549; Observed: 549. The *R* and *S* bromoalkylsulfonamides were similarly converted to give enantiomerically enriched products.

To a stirred solution of imidazole (82 mg, 1.2 mmol) in anhydrous THF(5.0 mL) was added 2.0 M *n*-BuLi Solution in hexanes (600 μL 1.2 mmol). The reaction mixture was stirred at room temperature for 30 min, and a solution of bromoalkyl sulfonamide derivative (220 mg, 0.34 mmol in 5 mL of THF) was added. The reaction mixture was stirred at room temperature for 6 h, then quenched with saturated bicarbonate solution, extracted with ethyl acetate (2 x 25 mL), the combined organic layer were washed with water (2 x 20 mL), dried with MgSO_4 , filtered and concentrated to give 200 mg of crude product which was purified by SiO_2 chromatography (5% methanol in DCM) to yield 188 mg of product. R_f = 0.62 (9:1 DCM/methanol). ^1H NMR (CDCl_3 , 300 MHz) δ (ppm): 7.63-6.65 (m, 14H). 6.25-6.23 (m, 1H), 4.52-4.32 (m, 2H), 4.08-3.88 (m, 2H), 2.44-2.27 9m, 2H), 1.25-1.21 (overlapping d, 3H). ^{13}C NMR (75 MHz) (partial list of resolved lines) δ (ppm): 159.0, 155.81 139.3, 130.1, 137.4, 129.7, 129.4, 128.9, 119.1, 117.6 (d), 117.4 (d), 110.9, 64.1, 52.7, 43.6, 30.9, 18.4.LC-MS calculated for $\text{C}_{26}\text{H}_{24}\text{ClF}_2\text{N}_3\text{O}_3\text{S}$: 532; Observed: 532.

The compounds described in Examples 322-331 were prepared according to the scheme described in the previous example.

EXAMPLE 322

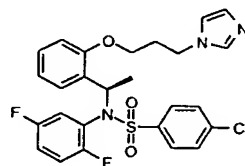
4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1-piperidinyl)propoxy]phenyl}propyl)benzenesulfonamide hydrochloride



- 5 $R_f = 0.38$ (10 % methanol in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): (t, 4H), 7.26-7.03 (m, 3H), 6.81 (br, 1H), 6.67-6.55 (m, 2H), 6.13-6.04 (m, 2H), 4.32-4.22 (m, 2H), 3.68-3.35 (m, 4H), 3.06 (br, 2H), 2.39-2.38 (m, 2H), 1.99-1.55 (m, 8H), 0.80 (d, 3H). MS calculated for $\text{C}_{29}\text{H}_{33}\text{ClF}_2\text{N}_2\text{O}_3\text{S}$, $[\text{MH}^+]$ 563: Observed: 563.

EXAMPLE 323

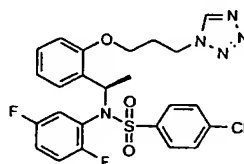
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride



- 10 $R_f = 0.46$ (10 % methanol in DCM), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 8.21 (s, 1H), 7.73-7.42 (m, 6H), 7.20-6.68 (m, 7H), 6.25 (m, 1H), 4.64 (m, 2H), 4.10 (br, 2H), 2.44 (m, 2H), 1.55 (br, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{24}\text{ClF}_2\text{N}_3\text{O}_3\text{S}$, $[\text{MH}^+]$ 532; Observed: 532.

EXAMPLE 324

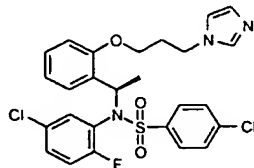
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-tetrazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide



- 20 $R_f = 0.57$ (19:1; DCM:methanol). ^1H NMR (CDCl_3) δ (ppm): 8.98 (s, 1H), 7.67-7.62 (m, 2H), 7.48-7.42 (m, 2H), 7.21-7.19 (m, 1H), 6.95-6.52 (m, 5.5H), 6.35-6.28 (m, 1.5H), 5.29-5.06 (m, 1H), 4.95-4.87 (m, 1H), 4.17-3.95 (m, 1H), 2.68-2.50 (m, 2H), 1.54-1.46 (br, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{22}\text{ClF}_2\text{N}_5\text{O}_3\text{S}$: 534. Observed: 536 (MNa^+).

EXAMPLE 325

4-chloro-N-(5-chloro-2-fluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride

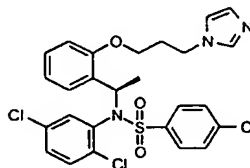


5 $R_f = 0.15$ (5 % methanol in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.81-6.59 (m, 14H), 6.20 (s, 1H), 4.54-4.29 (m, 2H), 4.08-3.90 (m, 2H), 2.39-2.14 (m, 2H), 1.63 (br, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{24}\text{Cl}_2\text{FN}_3\text{O}_3\text{S}$, $[\text{MH}^+]$ 548; Observed: 548.

EXAMPLE 326

4-chloro-N-(2,5-dichlorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride

10

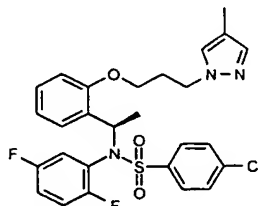


$R_f = 0.72$ (10 % methanol in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.64 (d, 2H), 7.53 (d, 2H), 7.41-6.66 (m, 10H), 6.14 (m, 1H), 4.32 (m, 2H), 3.94 (m, 2H), 2.30 (m, 2H), 1.63-1.49 (dd, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{24}\text{Cl}_3\text{N}_3\text{O}_3\text{S}$, $[\text{MH}^+]$ 564; Observed: 564.

15

EXAMPLE 327

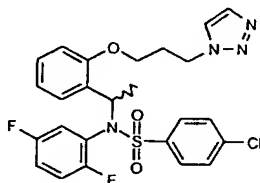
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(4-methyl-1H-pyrazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide



20 $R_f = 0.32$ (19:1 DCM:methanol). ^1H NMR (CDCl_3) δ (ppm): 7.65-7.62 (d, 2H), 7.53(s, 0.5H), 7.47(s, 0.5H), 7.40-7.38 (d, 2H), 7.21-7.16 (t, 1H), 6.92-6.67 (m, 5.5H), 6.28-6.23(m, 1.5H), 4.42-4.25 (m, 2H), 4.07-3.89 (m, 2H), 2.45-2.27 (m, 2H), 2.24 (s, 1.5H), 2.22(s, 1.5H), 1.53 (d, 3H), LC-MS calculated for $\text{C}_{27}\text{H}_{26}\text{ClF}_2\text{N}_3\text{O}_3\text{S}$: 546. Observed: 546.2.

EXAMPLE 328

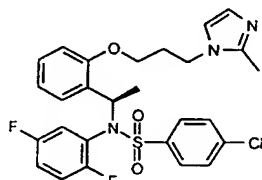
4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-1,2,3-triazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide



5 $R_f = 0.32$ (3:1; hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.66-7.61 (m, 4H), 7.39-7.35 (m, 2H), 7.19-7.10 (m, 1H), 6.92-6.65 (5.5H), 6.15-6.11 (m, 1.5H), 4.89-4.81 (m, 2H), 4.10-4.02 (m, 1H), 3.95-3.87 (m, 1H), 2.58-2.47 (m, 2H), 1.57 (d, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{23}\text{ClF}_2\text{N}_4\text{O}_3\text{S}$: 533. Observed: 230 ($\text{M}^+ - 303$).

EXAMPLE 329

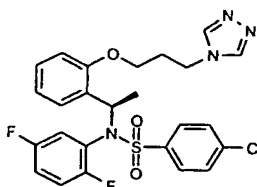
10 **4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(2-methyl-1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride**



15 $R_f = 0.31$ (19:1; DCM:methanol), ^1H NMR (CD_3OD) δ (ppm): 7.42-7.01 (m, 6H), 6.79-6.44 (m, 5.5H), 6.07-6.00 (m, 1.5H), 4.43-4.34 (m, 2H), 4.08-3.95 (m, 2H), 2.50 (s, 3H), 2.35-2.24 (m, 2H), 1.30 (m, 3H). LC-MS calculated for $\text{C}_{27}\text{H}_{26}\text{ClF}_2\text{N}_3\text{O}_3\text{S}$: 546. Observed: 546 (M^+).

EXAMPLE 330

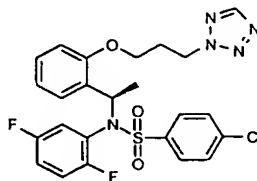
4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(4H-1,2,4-triazol-4-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride



20 $R_f = 0.28$ (19:1; DCM:methanol). ^1H NMR (CD_3OD) δ (ppm): 9.43 (s, 1H), 8.66 (s, 1H), 7.68-7.54 (m, 4H), 7.19-6.66 (m, 5.5H), 6.25-6.18 (m, 1.5H), 4.85-4.76 (m, 2H), 4.14-4.09 (m, 2H), 2.59-02.54 (m, 2H), 1.54 (br, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{23}\text{ClF}_2\text{N}_4\text{O}_3\text{S}$: 532. Observed: 532 (M^+).

EXAMPLE 331

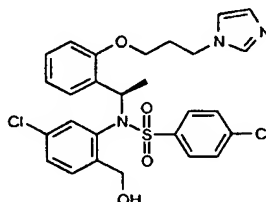
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(2H-tetraazol-2-yl)propoxy]phenyl}ethyl)benzenesulfonamide



- 5 $R_f = 0.25$ (4:1; hexanes:ethyl acetate), $^1\text{H NMR}$ (CDCl_3) δ (ppm): 8.89 (s, 1H), 7.67-7.61 (d, 2H), 7.41-7.33 (d, 2H), 7.13-7.10 (m, 1H), 6.93-6.66 (m, 6H), 6.23-6.21 (m, 1H), 5.23-5.09 (m, 2H), 4.19-4.09 (m, 1H), 4.00-3.93 (m, 1H), 2.66-2.56 (m, 2H), 1.56 (d, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{22}\text{ClF}_2\text{N}_5\text{O}_3\text{S}$: 533; observed 566 (MNa^+).

EXAMPLE 332

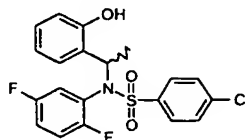
- 10 **4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide**



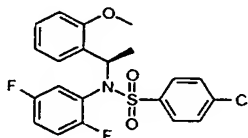
- 15 $R_f = 0.33$ (19:1; DCM:methanol). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.66-7.63 (m, 3H), 7.58-7.50 (m, 2H), 7.39 (m, 2H), 7.18 (m, 1H), 7.08 (m, 2H), 6.84 (d, 1H), 6.64 (t, 1H), 6.58 (s, 1H), 6.43-6.34 (m, 2H), 4.51-4.41 (m, 2H), 4.15-3.91 (m, 3H), 3.53 (d, 1H), 2.42 (m, 2H), 1.88 (m, 1H), 1.42 (d, 3H). LC-MS calculated for $\text{C}_{27}\text{H}_{27}\text{Cl}_2\text{N}_3\text{O}_4\text{S}$: 565; Observed: 565 (M^+).

EXAMPLE 333

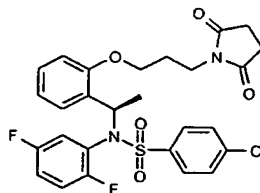
4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-hydroxyphenyl)ethyl]benzenesulfonamide



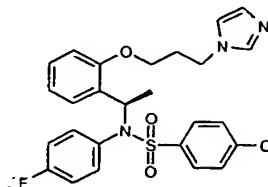
- 20 $R_f = 0.30$ (6:1; hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.82-7.79 (m, 2H), 7.60-7.50 (m, 2H), 7.33-6.91 (m, 6.5H), 6.33-6.19 (m, 0.5H), 5.30 (q, 1H), 1.36-1.25 (br, 3H). LC-MS calculated for $\text{C}_{20}\text{H}_{16}\text{ClF}_2\text{NO}_3\text{S}$: 423. Observed 446 (MNa^+).

EXAMPLE 334**4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-methoxyphenyl)ethyl]benzenesulfonamide**

5 $R_f = 0.32$ (15:1 hexanes: ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.66-7.63 (m, 2H), 7.39-7.37 (m, 2H), 7.18-7.15 (m, 1H), 6.96-6.66 (m, 5.5H), 5.81 (br, 1.5H), 1.67 (s, 1.5H), 1.57 (s, 1.5H).

EXAMPLE 335**4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(2,5-dioxo-1-pyrrolidinyl)propoxy]phenyl}ethyl)benzenesulfonamide**

10 $R_f = 0.46$ (3:1; hexanes:ethyl acetate). ^1H NMR CDCl_3 δ : 7.65-7.63 (d, 2H), 7.39-7.36 (d, 2H), 7.20-7.14 (m, 1H), 6.95-6.37 (m, 6H), 6.05 (m, 1H), 4.06-3.74 (m, 4H), 2.73 (s, 4H), 2.20-2.12(p, 2H), 1.56(d, 3H), LC-MS calculated for $\text{C}_{27}\text{H}_{25}\text{ClF}_2\text{N}_2\text{O}_5\text{S}$: 563.01 . Observed 260 ($\text{M}^+ - 303$).

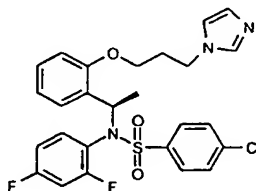
EXAMPLE 336**4-chloro-N-(4-fluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride**

15 $R_f = 0.34$ (5 % methanol in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm) : 7.60 (s, 1H), 7.51 (d, 2H), 7.35 (d, 2H), 7.08-6.94 (m, 2H), 6.89-6.76 (m, 3H), 6.54-6.46 (m, 2H), 6.35 (d, 1H), 6.24 (dt, 1H), 6.12 (q, 1H), 4.44-4.24 (m, 2H), 4.03-3.97 (m, 1H), 3.86-3.79 (m, 1H), 2.39-2.16 (m, 2H), 1.43 (d, 3H).

20 LC-MS calculated for $\text{C}_{26}\text{H}_{25}\text{ClFN}_3\text{O}_3\text{S}$, $[\text{MH}^+]$ 514; Observed: 514.

EXAMPLE 337

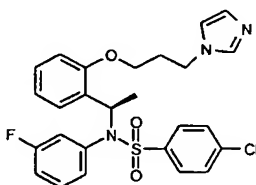
4-chloro-N-(2,4-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride



5 $R_f = 0.43$ (5% methanol in CH_2Cl_2) ^1H NMR (300MHz CD_3OD) δ (ppm): 7.88 (s, 1H), 7.72-7.69 (m, 2H), 7.51-7.48 (m, 2H), 7.40-7.27 (m, 2H), 7.17-7.11 (m, 1H), 7.04 (br, 1H), 7.00-6.94 (m, 1H), 6.84-6.49 (m, 4H), 6.28-6.21 (q, 1H), 4.56-4.37 (m, 2H), 4.01-3.89 (m, 2H), 2.36-2.27 (m, 2H), 1.46-1.43 (m, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{24}\text{ClF}_2\text{N}_3\text{O}_3\text{S}$ $[\text{MH}^+]$ 532; Observed: 532.

EXAMPLE 338

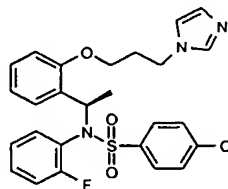
10 4-chloro-N-(3-fluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride



15 $R_f = 0.29$ (5% methanol in CH_2Cl_2) ^1H NMR (300MHz CD_3OD) δ (ppm): 7.80 (s, 1H), 7.70-7.65 (m, 2H), 7.56-7.52 (m, 2H), 7.27 (s, 1H), 7.24-7.17 (m, 1H), 7.01-6.85 (m, 4H), 6.71-6.66 (m, 4H), 6.36-6.29 (q, 1H), 4.64-4.43 (m, 2H), 4.21-4.14 (m, 1H), 4.05-3.98 (m, 1H), 2.58-2.30 (m, 2H), 1.68-1.51 (m, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{25}\text{ClFN}_3\text{O}_3\text{S}$ $[\text{MH}^+]$ 514; Observed: 514.

EXAMPLE 339

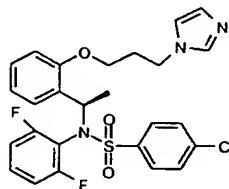
20 4-chloro-N-(2-fluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride



$R_f = 0.33$ (5% methanol in CH_2Cl_2) ^1H NMR (300MHz CD_3OD) δ (ppm): 7.68-6.47 (m, 15H), 6.27-6.08 (q, 1H), 4.43-4.27 (m, 2H), 3.88 (br, 2H), 2.27-2.14 (m, 2H), 1.41 (br, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{25}\text{ClFN}_3\text{O}_3\text{S}$ $[\text{MH}^+]$ 514; Observed: 514.

EXAMPLE 340

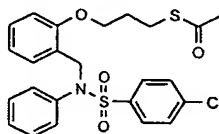
5 **4-chloro-N-(2,6-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride**



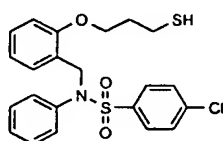
10 $R_f = 0.35$ (5% methanol in CH_2Cl_2) ^1H NMR (300MHz CD_3OD) δ (ppm): 7.54-7.25 (m, 6H), 7.08-6.34 (m, 8H), 6.13-5.97 (q, 1H), 4.36-4.23 (m, 2H), 3.97-3.78 (br, 2H), 2.20-2.10 (br, 2H), 1.35-1.25 (m, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{24}\text{ClF}_2\text{N}_3\text{O}_3\text{S}$ $[\text{MH}^+]$ 532; Observed: 532.

EXAMPLE 341

S-{3-[2-(((4-chlorophenyl)sulfonyl)anilino)methyl]phenoxy}propyl} ethanethioate

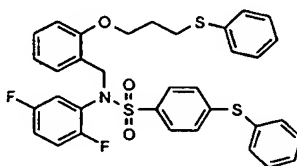


15 To a stirred solution of N-2-(3-bromopropoxy)benzyl 4-chlorobenzenesulfanilide (200 mg, 0.4 mmol) in DMF (5 mL) was added the potassium salt of thio acetic acid (92 mg, 0.81 mmol). The reaction mixture was then warmed to 60 °C. After 3 h, the reaction mixture was cooled to room temperature, diluted with ethyl acetate (25 mL), washed with saturated bicarbonate solution (3x 10 mL) and saturated brine (2x 10 mL), dried with MgSO_4 , filtered and concentrated under reduced pressure to isolate a colorless oil which was purified by SiO_2 chromatography (7:1, hexanes:ethyl acetate) to afford the desired product (130 mg, y: 63%). $R_f = 0.25$ (20% ethyl acetate/hexanes) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.60-7.56 (m, 2H), 7.46-7.42 (m, 2H), 7.36 (dd, 1H), 7.23-7.7.12 (dd, 2H), 6.85 (t, 1H), 6.70 (d, 1H), 4.82 (s, 2H), 3.85 (t, 2H), 2.95 (t, 2H), 2.33 (s, 3H), 1.92 (q, 2H), ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 196.0, 156.7, 139.6, 139.4, 137.5, 130.7, 129.5, 129.3, 129.3, 128.3, 124.5, 121.0, 111.3, 66.4, 49.8, 31.1, 29.6, 26.2.

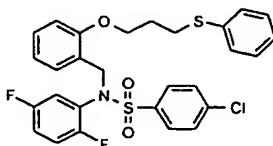
EXAMPLE 342**4-chloro-N-phenyl-N-[2-(3-sulfanylpropoxy)benzyl]benzenesulfonamide**

A stirred solution of thio acetate analog prepared above (100 mg, 0.2 mmol) at °C in ethanol (5 mL) was vigorously degassed for 0.5 h, then a solution of degassed 1.0 N NaOH (0.4 mL, 0.4 mmol) was added. The reaction mixture was allowed stir at 0 °C for 1h warmed to room temperature stirred at room temperature for 1h, then diluted with degassed ethyl acetate(20 mL), washed with saturated bicarbonate solution (3x 10 mL), 10% aqueous HCl (3x 10 mL), dried with MgSO₄, filtered and concentrated under reduced pressure to isolate a white solid. The crude material was purified by chromatography on SiO₂ (4:1 hexanes:ethyl acetate) to give 40 mg of product (y: 44%). R_f = 0.25 (20% ethyl acetate/hexanes) ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.58-7.56 (m, 2H), 7.47-7.54 (m, 2H), 7.34-7.14 (m, 5H), 6.99 (m, 2H), 6.87-6.73 (dt, 2H), 4.78 (s, 2H), 3.92 (t, 2H), 2.63 (q, 2H), 1.96 (q, 2H), 1.35 (t, 1H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 159.1, 141.9, 141.8, 139.9, 133.1, 131.8, 131.8, 131.7, 131.6, 130.6, 126.7, 123.2, 113.7, 68.2, 52.2, 35.8, 24.0.

The following compounds were prepared according to the scheme described in the previous example.

EXAMPLE 343**N-(2,5-difluorophenyl)-4-(phenylsulfanyl)-N-{2-[3-(phenylsulfanyl)propoxy]benzyl}benzenesulfonamide**

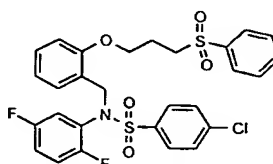
R_f = 0.54 (4:1 hexanes:ethyl acetate), ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.63 (d, 2H), 7.54-7.50 (m, 5H), 7.33-7.26 (m, 6H), 7.18 (t, 5H), 6.97 (m, 1H), 6.87-6.79 (m, 2H), 4.70 (s, 2H), 3.94 (t, 2H), 3.08 (t, 2H), 1.90-1.86 (m, 2H).

EXAMPLE 344**4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(phenylsulfanyl)propoxy]benzyl}benzenesulfonamide**

$R_f = 0.45$ (6:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, DMSO) δ (ppm): 7.72 (q, 4H), 7.34-7.18 (m, 8H), 7.00-6.98 (m, 2H), 6.89-6.80 (m, 2H), 4.73 (s, 2H), 3.95 (t, 2H), 3.09 (t, 2H), 1.91-1.87 (m, 2H).

EXAMPLE 345

5 **4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(phenylsulfonyl)propoxy]benzyl}benzenesulfonamide**

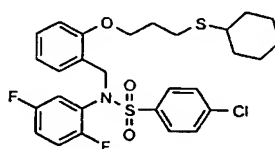


$R_f = 0.40$ (3:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.96 (d, 2H), 7.68-7.54 (m, 5H), 7.47 (d, 2H), 7.19-7.10 (m, 2H), 6.93-6.68 (m, 5H), 4.77 (s, 2H), 3.97 (t, 2H), 3.38 (t, 2H), 2.24-2.15 (m, 2H).

10

EXAMPLE 346

4-chloro-N-{2-[3-(cyclohexylsulfanyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide

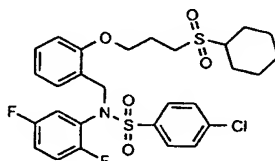


$R_f = 0.26$ (5% methanol in DCM), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.66 (d, 2H), 7.47 (m, 2H), 7.28-7.15 (m, 1H), 7.00 (d, 1H), 6.90 (m, 2H), 6.75 (m, 3H), 4.81 (s, 2H), 3.92 (m, 2H), 2.66 (m, 3H), 1.94 (m, 4H), 1.75 (m, 2H), 1.60 (m, 2H), 1.28 (m, 4H).

15

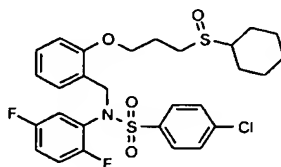
EXAMPLE 347

4-chloro-N-{2-[3-(cyclohexylsulfonyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide



$R_f = 0.29$ (3:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.65 (d, 2H), 7.48 (d, 2H), 7.18 (t, 1H), 7.80 (d, 2H), 6.90 (m, 2H), 6.76 (m, 3H), 4.78 (s, 2H), 4.10 (t, 2H), 3.29 (t, 2H), 2.94 (m, 1H), 2.35 (m, 2H), 2.22 (d, 2H), 1.90 (m, 2H), 1.72-1.19 (m, 6H). MS calculated for $\text{C}_{28}\text{H}_{30}\text{ClF}_2\text{NO}_5\text{S}_2$, $[\text{MNa}^+]$ 620; Observed: 620.

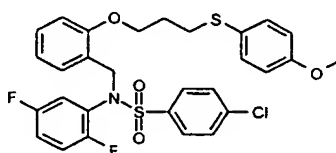
20

EXAMPLE 348**4-chloro-N-{2-[3-(cyclohexylsulfinyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide**

$R_f = 0.32$ (1:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.64 (d, 2H), 7.47 (d, 2H), 7.19 (t, 1H), 7.08 (d, 2H), 6.92-6.87 (m, 2H), 6.80-6.76 (m, 3H), 4.79 (s, 2H), 4.16-3.98 (m, 2H), 3.12-3.03 (m, 1H), 2.87-2.78 (m, 1H), 2.67-2.60 (m, 1H), 2.34 (m, 2H), 2.14 (d, 1H), 1.95-1.69 (m, 3H), 1.57-1.24 (m, 6H). MS calculated for $\text{C}_{28}\text{H}_{30}\text{ClF}_2\text{NO}_4\text{S}_2$, $[\text{MH}^+]$ 582; Observed: 582.

EXAMPLE 349

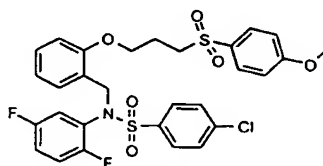
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-methoxyphenyl)sulfanyl]propoxy}benzyl)benzenesulfonamide



$R_f = 0.44$ (6:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.67-7.64 (m, 2H), 7.48-7.44 (m, 2H), 7.35-7.32 (m, 2H), 7.31-7.15 (m, 3H), 6.91-6.70 (m, 8H), 4.77 (m, 2H), 3.94-3.86 (m, 2H), 3.77 (m, 3H), 2.97-2.92 (m, 2H), 1.97-1.88 (m, 2H). MS calculated for $\text{C}_{29}\text{H}_{26}\text{ClF}_2\text{NO}_4\text{S}_2$, $[\text{MNa}^+]$ 612; Observed: 612.

EXAMPLE 350

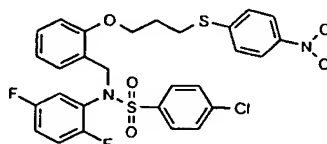
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-methoxyphenyl)sulfonyl]propoxy}benzyl)benzenesulfonamide



$R_f = 0.42$ (2:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.87 (d, 2H), 7.63 (d, 2H), 7.47 (d, 2H), 7.26-7.11 (m, 2H), 7.00 (d, 2H), 6.91-6.75 (m, 4H), 6.69 (d, 1H), 4.74 (s, 2H), 3.96 (t, 2H), 3.86 (s, 3H), 3.36-3.31 (m, 2H), 2.22-2.13 (m, 2H). MS calculated for $\text{C}_{29}\text{H}_{26}\text{ClF}_2\text{NO}_6\text{S}_2$, $[\text{MNa}^+]$ 644; Observed: 644.

EXAMPLE 351

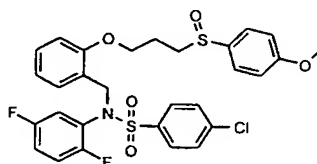
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-nitrophenyl)sulfonyl]propoxy}benzyl)benzenesulfonamide



5 $R_f = 0.40$ (6:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 8.12-8.09 (m, 2H), 7.67-7.63 (m, 2H), 7.49-7.45 (m, 2H), 7.41-7.37 (m, 2H), 7.22-7.16 (m, 1H), 7.12-7.09 (m, 1H), 6.91-6.74 (m, 5H), 4.82 (s, 2H), 4.05 (t, 2H), 3.32 (t, 2H), 2.19 (m, 2H).

EXAMPLE 352

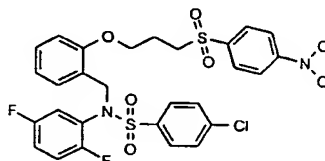
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-methoxyphenyl)sulfinyl]propoxy}benzyl)benzenesulfonamide



10 $R_f = 0.23$ (1:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.66-7.54 (m, 4H), 7.49 (d, 2H), 7.20-7.11 (m, 2H), 7.03 (d, 2H), 6.94-6.76 (m, 4H), 6.71 (d, 1H), 4.76 (s, 2H), 4.05-3.84 (m, 5H), 3.15-2.90 (m, 2H), 2.26-2.00 (m, 2H). MS calculated for $\text{C}_{29}\text{H}_{26}\text{ClF}_2\text{NO}_5\text{S}_2$, $[\text{MNa}^+]$ 628;
15 Observed: 628.

EXAMPLE 353

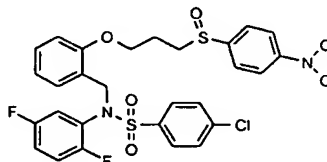
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-nitrophenyl)sulfonyl]propoxy}benzyl)benzenesulfonamide



20 $R_f = 0.56$ (2:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 8.40 (d, 2H), 8.25 (d, 2H), 7.59 (d, 2H), 7.48 (d, 2H), 7.19-7.14 (t, 1H), 6.89-6.82 (m, 3H), 6.75-6.64 (m, 3H), 4.73 (s, 2H), 4.1 (t, 2H), 3.65 (m, 2H), 2.38-2.33 (m, 2H).

EXAMPLE 354

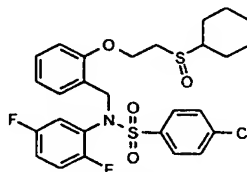
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-nitrophenyl)sulfinyl]propoxy}benzyl)benzenesulfonamide



- 5 $R_f = 0.53$ (1:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 8.36 (d, 2H), 7.93 (d, 2H), 7.64 (d, 2H), 7.50 (d, 2H), 7.17 (m, 1H), 6.91-6.80 (m, 3H), 6.74-6.65 (m, 3H), 4.76 (s, 2H), 4.19-4.02 (m, 2H), 3.56-3.47 (m, 1H), 3.23-3.14 (m, 1H), 2.47-2.41 (m, 1H), 2.17-2.13 (m, 1H).

EXAMPLE 355

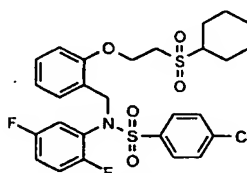
4-chloro-N-{2-[2-(cyclohexylsulfinyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide



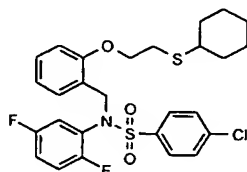
- 10 $R_f = 0.35$ (1:2 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.65 (d, 2H), 7.47 (d, 2H), 7.22-7.11 (m, 2H), 6.94-6.80 (m, 5H), 4.84 (d, 1H), 4.70 (d, 1H), 4.47-4.27 (m, 2H), 3.19-3.10 (m, 1H), 2.94 (dt, 1H), 2.65 (tt, 1H), 2.14 (d, 1H), 2.04-1.88 (m, 3H), 1.73 (m, 1H), 1.59-1.25 (m, 4H).

EXAMPLE 356

- 15 **4-chloro-N-{2-[2-(cyclohexylsulfonyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide**



- $R_f = 0.30$ (3:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.65 (d, 2H), 7.47 (d, 2H), 7.26-7.18 (m, 2H), 6.97-6.81 (m, 5H), 4.78 (s, 2H), 4.35 (t, 2H), 3.38 (t, 2H), 2.92 (tr, 1H), 2.20 (d, 2H), 2.05 (m, 2H), 1.74-1.55 (m, 3H), 1.334-1.20 (m, 3H).

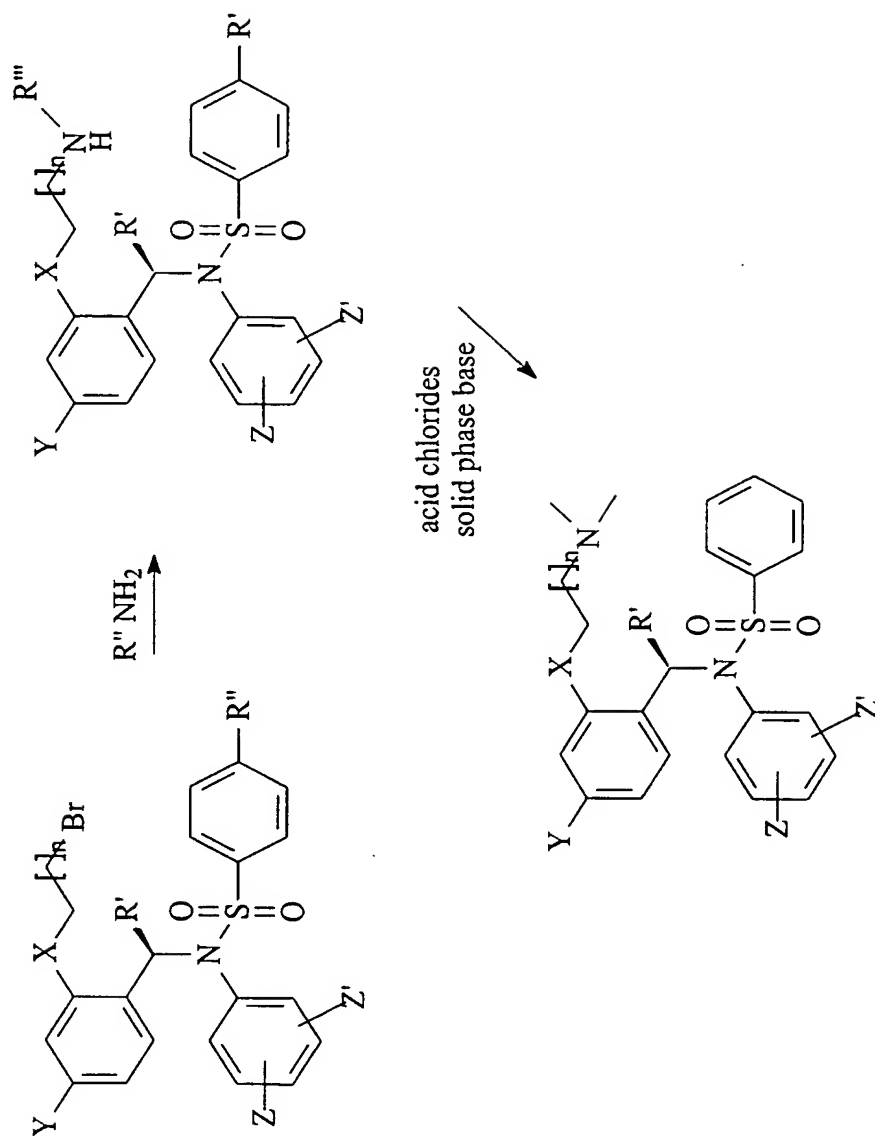
EXAMPLE 357**4-chloro-N-{2-[2-(cyclohexylsulfanyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide**

- 5 $R_f = 0.30$ (15:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.67 (d, 2H), 7.56 (d, 2H), 7.34 (d, 1H), 7.19 (t, 1H), 6.95-6.86 (m, 4H), 6.72 (d, 1H), 4.79 (s, 2H), 3.93 (t, 2H), 2.74 (t, 2H), 2.67 (m, 1H), 1.95 (br, 2H), 1.77 (br, 2H), 1.63-1.27 (m, 6H).

EXAMPLE 358

- 10 The compounds described in Examples 359-373 were prepared according to the preparative scheme outlined in the previous example.

SCHEME 358

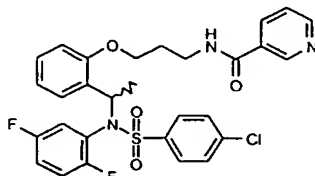


$R' = H, CH_3, CH_2CH_3$
 $R'' = F, Cl, Br$
 $R''' = H, CH_3, CH_2CH_3$

$X = O, CH_2$
 $n = 0, 1, 2, \text{or } 3$
 $Y = H, F$

EXAMPLE 359

N-{3-[2-(1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]phenoxy]propyl}nicotinamide



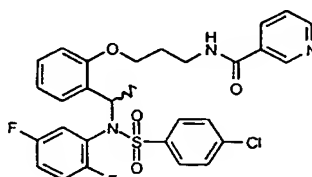
5

$R_f = 0.43$ (19:1; DCM:methanol). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 9.08 (s, 1H), 8.68 (m, 1H), 8.19-8.15 (m, 1H), 7.63-7.60 (m, 2H), 7.42-7.47 (m, 4H), 6.91-6.66 (m, 6H), 6.20 (q, 1H), 4.22-4.13 (m, 2H), 3.89-3.85 (m, 2H), 2.46-2.43 (m, 1H), 2.28-2.19 (m, 1H), 1.44 (d, 3H). LC-MS calculated for $\text{C}_{29}\text{H}_{26}\text{ClF}_2\text{N}_3\text{O}_4\text{S}$: 586; observed: 586 (M^+).

10

EXAMPLE 360

N-{3-[2-(1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]phenoxy]propyl}-N-methylnicotinamide

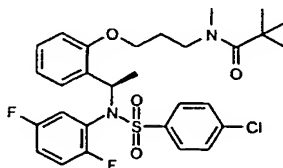


$R_f = 0.60$ (9:1 CH_2Cl_2 :methanol) $^1\text{H NMR}$ (300MHz CDCl_3) δ (ppm): 8.69-8.59 (m, 2H), 7.79-6.11 (m, 13H), 5.80-5.68 (m, 1H), 4.28-3.41 (m, 4H), 3.25-2.97 (d, 3H), 2.50-1.98 (br, 2H), 1.66-1.35 (m, 3H). LC-MS calculated for $\text{C}_{30}\text{H}_{28}\text{ClF}_2\text{N}_3\text{O}_4\text{S}$ [MH^+]: 600; Observed [MH^+]: 600.

15

EXAMPLE 361

N-{3-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]phenoxy]propyl}-N,2,2-trimethylpropanamide

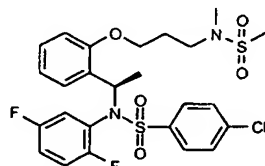


20

$R_f = 0.28$ (3:1; hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.64-7.61 (m, 2H), 7.39-7.36 (m, 2H), 7.21-7.16 (m, 1H), 6.92-6.65 (m, 5.5H), 6.36-6.14 (m, 1.5H), 4.16-3.95 (m, 2H), 3.75-3.57 (m, 2H), 3.18 (m, 3H), 2.23-2.05 (m, 2H), 1.57 (d, 3H), 1.29 (s, 9H). LC-MS- calculated for $\text{C}_{29}\text{H}_{33}\text{ClF}_2\text{N}_2\text{O}_4\text{S}$: 579. Observed: 579 (M^+).

EXAMPLE 362

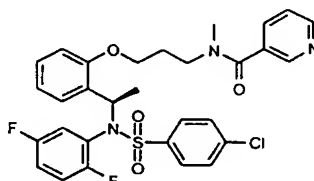
4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{3-[methyl(methylsulfonyl)amino]propoxy}phenyl)ethyl]benzenesulfonamide



5 $R_f = 0.25$ (2:1 hexanes:ethyl acetate) $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.65-7.62 (d, 2H), 7.42-7.39 (d, 2H), 7.20-7.17 (m, 1H), 6.91-6.34 (m, 6H), 6.19 (q, 1H), 4.20-4.06 (m, 2H), 3.64-3.55 (m, 2H), 2.96 (s, 3H), 2.84 (s, 3H), 2.25-2.19 (m, 2H), 1.53 (d, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{27}\text{ClF}_2\text{N}_2\text{O}_5\text{S}_2$: 573; Observed: 573 (M^+).

EXAMPLE 363

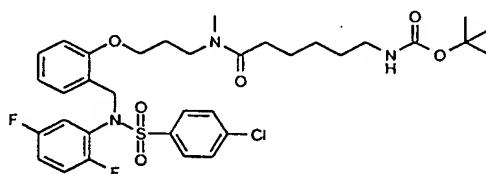
10 **N-{3-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]phenoxy}propyl}-N-methylnicotinamide hydrochloride**



15 $R_f = 0.56$ (19:1; DCM:methanol). $^1\text{H NMR}$ (CD_3OD) δ (ppm): 8.55-8.45 (m, 2H), 7.92-6.08 (overlapping m, 12H), 5.45 (q, 1H), 4.08-3.45 (m, 4H), 3.10 (s, 1.5H), 2.99 (s, 1.5H), 2.19-2.06 (m, 2H), 1.47 (d, 1.5H), 1.34 (d, 1.5H). LC-MS calculated for $\text{C}_{30}\text{H}_{28}\text{ClF}_2\text{N}_3\text{O}_4\text{S}$: 600; Observed: 600 (M^+).

EXAMPLE 364

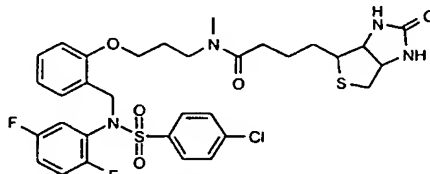
tert-butyl 6-[[3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl](methyl)amino]-6-oxohexylcarbamate



20 $R_f = 0.33$ (1:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.67-7.64 (d, 2H), 7.48-7.45 (d, 2H), 7.22-7.08 (m, 2H), 6.91-6.73(m, 5H), 4.81(s, 2H), 4.53 (br, 1H), 3.94-3.86 (m, 2H), 3.58-5.53 (m, 2H), 3.12-2.95 (m overlaps d, 5H), 2.30 (t, 2H), 2.04-2.96 (m, 2H), 1.69-1.23 (m, 13H).

EXAMPLE 365

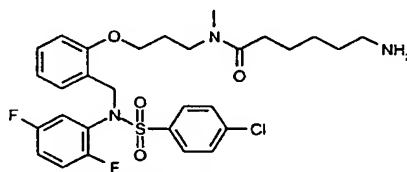
N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl)phenoxy]propyl}-N-methyl-5-(2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide



- 5 $R_f = 0.57$ (10:1; DCM:methanol). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.68-7.65 (d, 2H), 7.49-7.46(m, 2H), 7.22-7.05 (m, 2H), 6.90-6.73 (m, 5H), 5.13(br, 0.5H), 5.06 (br, 0.5H), 4.82-4.81 (d, 2H), 4.63-4.59 (m, 1H), 4.49-4.47 (m, 1H), 4.31-4.24 (m, 1H), 3.96-3.87 (m, 2H), 3.59-3.56(m, 2H), 3.17-2.87 (m, 5H), 2.73-2.67 (m, 1H), 2.40-2.32 (m, 2H), 2.08-1.96 (m, 2H), 1.70-1.65 (m, 6H).

EXAMPLE 366

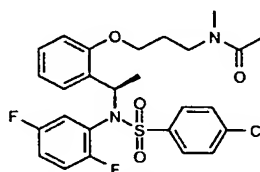
- 10 **6-amino-N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl)phenoxy]propyl}-N-methylhexanamide hydrochloride**



- 15 $R_f = 0.56$ (6:1;DCM:methanol). $^1\text{H NMR}$ (CD_3OD) δ (ppm): 7.76-7.52 (m, 2H), 7.65-7.61 (m, 2H), 7.22-7.02 (m, 4H), 6.93-6.75 (m, 3H), 4.88 (d overlaps HOD, 2H), 4.01 (t, 1H), 3.93 (t, 1H), 3.71 (t, 1H), 3.63 (t, 1H), 3.12 (s, 1.5H), 2.99(s, 1.5H), 2.93 (t, 1H), 2.86 (t, 1H), 2.49-2.42 (m, 2H), 2.12-2.00 (m, 2H), 1.71-1.60 (m, 4H), 1.35-1.32 (m, 2H).

EXAMPLE 367

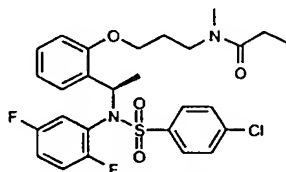
N-{3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methylacetamide



- 20 $R_f = 0.38$ (1:1; hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.65-7.62 (m, 2H), 7.40-7.37 (m, 2H), 7.22-7.16 (m, 1H), 6.91-6.64 (m, 5.5H), 6.35-6.16 (m, 1.5H), 4.12-3.95 (m, 2H), 3.77-3.57 (m, 2H), 3.10 (s, 1.5H), 3.00(s, 1.5H), 2.17-2.10 (m overlaps two s, 5H), 1.58-1.53 (m, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{27}\text{ClF}_2\text{N}_2\text{O}_4\text{S}$: 537. Observed 537 (M^+).

EXAMPLE 368

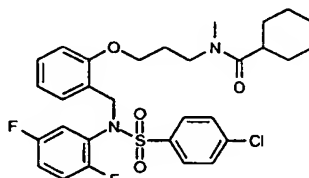
N-{4-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl)phenoxy]butyl}-N-methylpropanamide



5 $R_f = 0.4$ (1:1 hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.63-7.62 (d, 2H), 7.39-7.35 (m, 3H), 7.19-7.15 (m, 2H) 6.91-6.64 (m, 5H), 6.06 (m, 1H), 4.13-4.00 (m, 2H), 3.49-3.39(m, 2H), 3.01-2.97 (d, 3H), 2.43-2.33(m, 2H), 1.85-1.83 (m, 4H), 1.57 (d, 3H), 1.17-1.11(dt, 3H). LC-MS calculated for $\text{C}_{28}\text{H}_{31}\text{ClF}_2\text{N}_2\text{O}_4\text{S}$: 565; Observed: 565 (M^+).

EXAMPLE 369

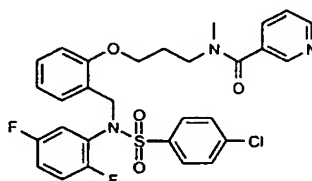
10 N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl)phenoxy]propyl}-N-methylcyclohexanecarboxamide



15 $R_f = 0.26$ (2:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.65 (m, 2H), 7.44 (d, 2H), 7.19-7.11 (m, 2H), 6.90-6.70 (m, 5H), 4.80 (d, 2H), 3.90-3.82 (m, 2), 3.58-3.50 (m, 2H), 2.91 (d, 3H), 2.49-2.42 (m, 1H), 2.02-1.90 (m, 2H), 1.77 -0.83 (m, 11H). MS calculated for $\text{C}_{30}\text{H}_{33}\text{ClF}_2\text{N}_2\text{O}_4\text{S}$, $[\text{MNa}^+]$ 613; Observed: 613.

EXAMPLE 370

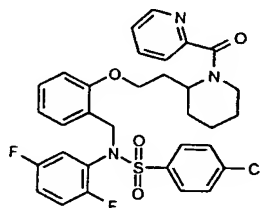
20 N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl)phenoxy]propyl}-N-methylnicotinamide



25 $R_f = 0.66$ (9:1 CH_2Cl_2 :methanol) $^1\text{H NMR}$ (300MHz CDCl_3) δ (ppm): 8.65-8.55 (m, 2H), 7.74-7.59 (m, 3H), 7.46-7.43 (d, 2H), 7.35-7.31 (m, 1H), 7.19-7.14 (m, 1H), 7.06-6.98 (m, 1H), 6.87-6.61 (m, 5H), 4.80-4.76 (br, 1H), 4.45 (br, 1H), 4.01-3.98 (t, 1H), 3.81-3.76 (m, 2H), 3.61-3.57 (m, 1H), 3.13-3.04 (d, 3H), 2.18-2.01 (m, 2H). LC-MS calculated for $\text{C}_{29}\text{H}_{26}\text{ClF}_2\text{N}_3\text{O}_4\text{S}$ $[\text{MH}^+]$ 586; Observed: 586.

EXAMPLE 371

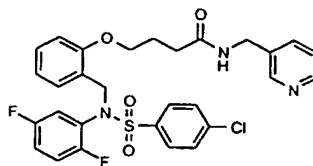
4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(3-pyridinylcarbonyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide



5 $R_f = 0.50$ (1:3 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 8.57 (m, 2H), 7.62-6.89 (m, 13H), 5.30-2.88 (m, 15H), 2.30-1.48 (m, 8H). MS calculated for $\text{C}_{32}\text{H}_{30}\text{ClF}_2\text{N}_3\text{O}_4\text{S}$, $[\text{MH}^+]$ 626; Observed: 626.

EXAMPLE 372

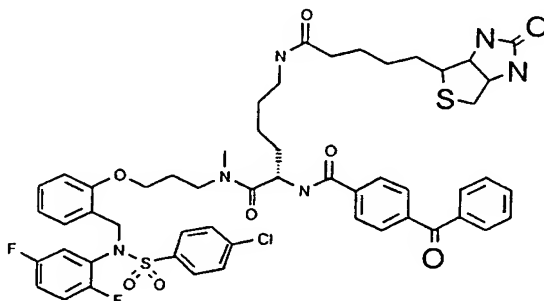
4-[2-(1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]phenoxy]-N-(3-pyridinylmethyl)butanamide hydrochloride



10 $R_f = 0.53$ (5% methanol in CH_2Cl_2) $^1\text{H NMR}$ (300MHz CD_3OD) δ (ppm) : 8.78 (s, 1H), 8.69-8.68 (d, 1H), 8.54-8.51 (d, 1H), 7.96-7.92 (m, 1H), 7.66-7.63 (d, 2H), 7.52-7.49 (d, 2H), 7.20-6.62 (m, 6H), 6.15-6.09 (q, 1H), 4.58 (br, 2H), 4.09-3.99 (m, 2H), 2.75-2.61 (m, 2H), 2.24-2.17 (m, 2H), 1.57-1.54 (d, 3H). LC-MS calculated for $\text{C}_{30}\text{H}_{28}\text{ClF}_3\text{N}_3\text{O}_4\text{S}$ $[\text{MH}^+]$ 600; Observed: 600.

EXAMPLE 373

4-benzoyl-N-((1S)-1-[[3-[2-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl]phenoxy]propyl](methyl)amino]carbonyl]-5-[[5-(2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanoyl]amino}pentyl)benzamide



20

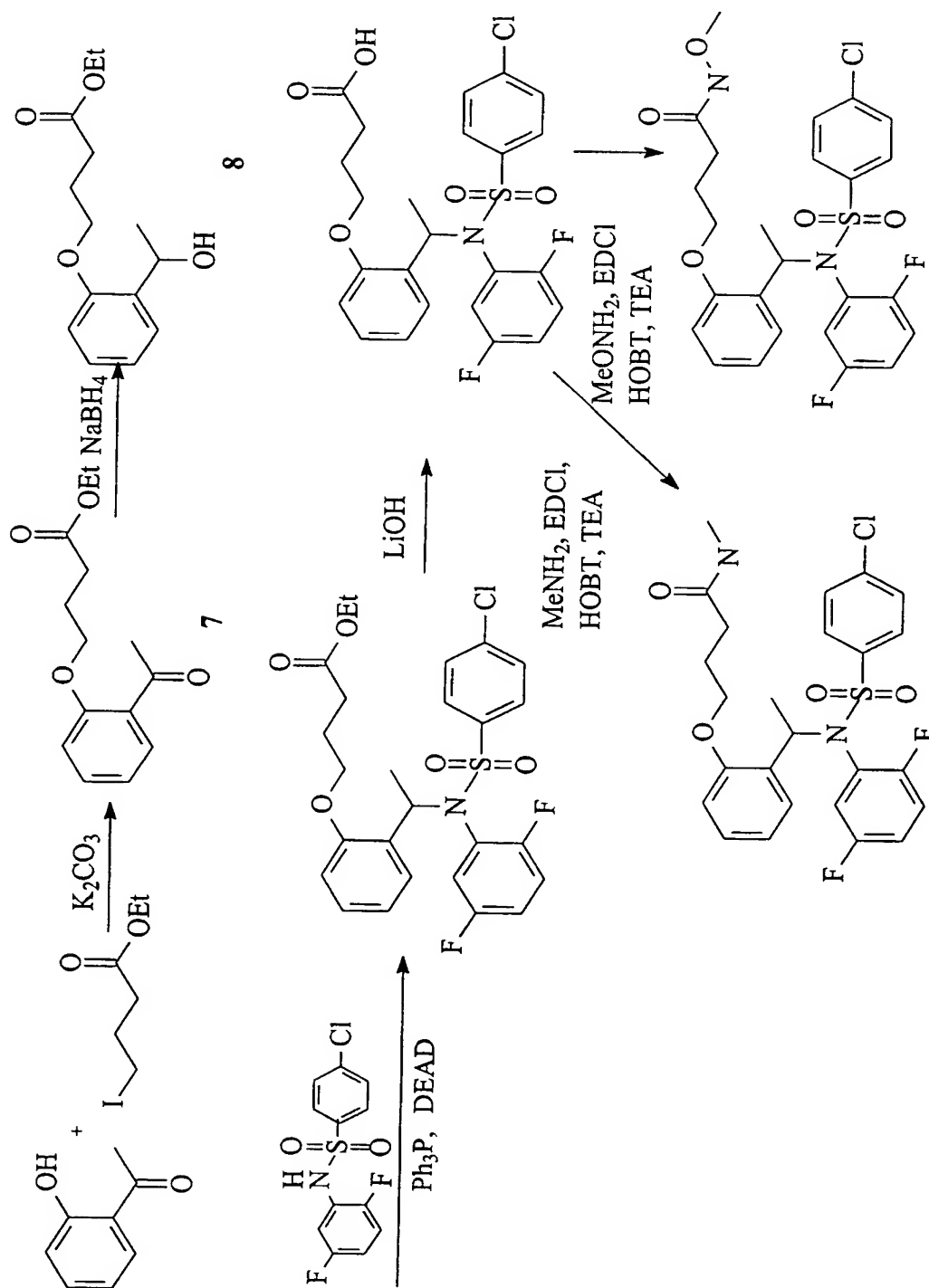
$R_f = 0.37$ (7 % Methanol in DCM), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 8.15-7.78 (m, 6H), 7.70-7.59 (m, 3H), 7.52-7.45 (m, 4H), 7.15 (t, 1H), 7.03 (d, 1H), 6.89-6.72 (m, 5H), 6.443-6.19 (m,

2H), 5.37 (m, 1H), 5.33 (s, 2H), 5.12 (m, 1H), 4.86-4.82 (m, 1H), 4.44 (m, 1H), 4.26 (m, 1H), 4.01-3.93 (m, 2H), 3.82-3.67 (m, 2H), 3.22-2.65 (m, 9H), 2.17-1.26 (m, 24H).

EXAMPLE 374

Numerous compounds according to the invention can be prepared employing the synthetic
5 scheme set forth in SCHEME 374.

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SCHEME 374

EXAMPLE 375

A suspension of 2-hydroxyphenone (10 mL, 83 mmol), 4-bromobutyric acid (16.6 mL, 116 mmol) and K_2CO_3 (14.4 g, 104 mmol) in acetone was refluxed at 56 °C for 64 h. The reaction mixture was acidified with 1 N HCl solution and the acidic solution was extracted with ethyl acetate (3 X 50 mL). The combined organic phase was washed with H_2O and sat. NaCl aqueous solution, dried over $MgSO_4$. The solution was filtered, concentrated the filtrate to obtain the crude product that purified by SiO_2 chromatography to isolate the desired product 7 (15.5 g, 75%) as white solid: R_f 0.46 (10:5, hexane-ethyl acetate); 1H NMR ($CDCl_3$, 300 MHz) δ 7.72 (dd, 1 H, $J = 7.6$ Hz, $J = 1.4$ Hz), 7.43 (td, 1 H, $J = 7.6$ Hz, $J = 1.2$ Hz), 6.96 (m, 2H), 4.13 (m, 4H), 2.62 (s, 3H), 2.54 (t, 2H, $J = 6.6$ Hz), 2.18 (m, 2H), 2.26 (t, 3H, $J = 7.2$ Hz).

Compound 7 in the reaction scheme outlined above (3.0 g, 12.0 mmol) was treated with $NaBH_4$ (227 mg, 6.0 mmol) in methanol (24 mL) solution in the presence of $CeCl_3 \cdot 7H_2O$ (89 mg, 0.24 mmol) at 25 °C for 10 min. The reaction was quenched with 5% HCl solution. The aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with H_2O and sat. NaCl aqueous solution, then dried over $MgSO_4$. Concentration and chromatography afforded compound 8 (3.0 g, 100%) as colorless gum: R_f 0.29 (10:5, hexane-ethyl acetate); 1H NMR ($CDCl_3$, 300 MHz) δ 7.48 (d, 1H, $J = 7.5$ Hz), 7.26 (t, 1H, $J = 7.6$ Hz), 7.05 (t, 1H, $J = 7.6$ Hz), 6.80 (d, 1H, $J = 8.1$ Hz), 5.26 (br s, 1H), 4.68 (s, 2H), 4.28 (q, 2H, $J = 7.2$ Hz), 4.06 (br s, 1H), 1.59 (d, 3H, $J = 6.6$ Hz), 1.33 (t, 3H, $J = 7.2$ Hz).

EXAMPLE 376

20 ethyl-4-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butanoate

DEAD (567 μ L, 3.6 mmol) was added dropwise to a solution of alcohol 8 (666 mg, 3.0 mmol), Triphenylphosphine (944 mg, 3.6 mmol) and sulfonamide (910 mg, 3.0 mmol) in toluene (10 mL) at 25 °C under Ar. The mixture was stirred for 40 h, then diluted with hexane-ethyl acetate solution (10:3). The generated precipitates were filtered and the filtrate was concentrated in vacuo. Chromatography 25 afforded the compound (1.16 g, 72%) as colorless gum: R_f 0.29 (10:2, hexane-ethyl acetate); 1H NMR ($CDCl_3$, 300 MHz) δ 7.62 (d, 2H, $J = 8.7$ Hz), 7.36 (d, 2H, $J = 8.7$ Hz), 7.18 (m, 1H), 6.38-6.95 (m, 6H), 6.01 (m, 1H), 4.17 (q, 2H, $J = 7.2$ Hz), 4.04 (m, 1H), 3.98 (m, 1H), 2.61 (t, 2H, $J = 7.0$ Hz), 2.17 (m, 2H), 1.58 (d, 3H, $J = 6.9$ Hz), 1.27 (t, 3H, $J = 7.0$ Hz); LCMS 3.86 min, m/z 556 ($M+H^+ + H_2O$, $C_{26}H_{26}ClF_2NO_5S$ requires 538.01).

30

EXAMPLE 377

4-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butanoic acid

A solution of ethyl 4-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl) phenoxy] butanoate (1.16 g, 2.2 mmol) in THF (5.2 mL), methanol (1.7 mL) and H_2O (1.7 mL) was treated with

LiOH·H₂O (91 mg, 2.2 mmol) at 25 °C for 3 h. The reaction was then quenched with 1 N HCl solution. The aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with H₂O and sat. NaCl aqueous solution, then dried over MgSO₄. Concentration and chromatography afforded the desired product (457 mg, 41%) as white crystal: m.p. 141.0 –142.0 °C; R_f 0.14 (10:10, hexane-ethyl acetate); ¹H NMR (CDCl₃, 300 MHz) δ 11.08 (br s, 1H), 7.62 (d, 2H, J = 8.4 Hz), 7.35 (d, 2H, J = 8.7 Hz), 7.16 (t, 1H, J = 7.5 Hz), 6.38-6.93 (m, 6H), 6.03 (br s, 1H), 4.06 (m, 2H), 2.70 (t, 2H, J = 7.0 Hz), 2.17 (m, 2H), 1.57 (d, 3H, J = 6.9 Hz); LCMS 3.05 min, m/z 527.2 (C₂₄H₂₂ClF₂NO₅S requires 509.95).

EXAMPLE 378

4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]-N-methylbutanamide

A mixture of acid 4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl) phenoxy] butanoic acid (107 mg, 0.21 mmol), HOBT (31 mg, 0.23 mmol), EDCI (44 mg, 0.23 mmol), Et₃N (88 μL, 0.63 mmol) and CH₃NH₂·HCl (16 mg, 0.23 mmol) in CH₂Cl₂ (1.0 mL) was stirred at 25 °C for 13 h. The mixture was diluted with ethyl acetate. The organic solution was washed with H₂O and sat. NaCl solution then dried over MgSO₄. Concentration and chromatography afforded the amide (107 mg, 97%) as colorless gum: R_f 0.32 (10:20, hexane-ethyl acetate); ¹H NMR (CDCl₃, 300 MHz) δ 7.64 (d, 2H, J = 6.9 Hz), 7.42 (d, 2H, J = 7.8 Hz), 7.18 (t, 1H, J = 8.7 Hz), 6.36-6.91 (m, 7H), 6.26 (q, 1H, J = 6.9 Hz), 4.13 (m, 1H), 4.05 (m, 1H), 2.78 (m, 4H), 2.57 (m, 1H), 2.23 (m, 2H), 1.55 (br s, 3H); LCMS m/z 524 (M+H⁺, C₂₅H₂₅ClF₂N₂O₄S requires 522.99).

EXAMPLE 379

4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]-N-methoxybutanamide

A mixture of 4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl) phenoxy] butanoic acid (107 mg, 0.21 mmol), HOBT (31 mg, 0.23 mmol), EDCI (44 mg, 0.23 mmol), Et₃N (88 μL, 0.63 mmol) and CH₃ONH₂·HCl (19 mg, 0.23 mmol) in CH₂Cl₂ (1.0 mL) was stirred at 25 °C for 13 h. The reaction mixture was diluted with ethyl acetate. The organic solution was washed with H₂O and sat. NaCl solution then dried over MgSO₄. Concentration and chromatography afforded the compound (94 mg, 83%) as colorless gum: R_f 0.20 (10:10, hexane-ethyl acetate); ¹H NMR (CDCl₃, 300 MHz) δ 9.50 (br s, 1H), 7.64 (br s, 2H), 7.43 (br s, 2H), 7.16 (m, 1H), 6.34-6.87 (m, 6H), 6.27 (q, 1H, J = 6.9 Hz), 4.14 (m, 1H), 4.06 (m, 1H), 3.74 (s, 3H), 2.72 (m, 1H), 2.51 (m, 1H), 2.26 (m, 2H), 1.54 (br s, 3H); LCMS 2.95, m/z 562 (M+Na⁺, C₂₅H₂₅ClF₂N₂O₅S requires 538.99).

EXAMPLE 380

Numerous compounds according to the invention can be prepared employing the general synthetic scheme set forth in SCHEME 380.

A suspension of 2-hydroxyphenone (10 mL, 83 mmol), ethyl iodoacetate (25.0 g, 117 mmol) and K_2CO_3 (12.6 g, 91 mmol) in acetone was refluxed at 60 °C for 28 h. The reaction mixture was then diluted with ether. The ether solution was washed with 1 N NaOH solution, H_2O and sat. NaCl aqueous solution, then dried over $MgSO_4$. Concentration and chromatography afforded compound 9 (8.76 g, 47%) as white solid: R_f 0.19 (10:2, hexane-ethyl acetate); 1H NMR ($CDCl_3$, 300 MHz) δ 7.76 (m, 1H), 7.42 (m, 1H), 7.04 (m, 1H), 6.82 (m, 1H), 4.70 (m, 2H), 4.28 (q, 2H, $J = 4.2$ Hz), 2.72 (s, 3H), 1.31 (t, 3H, $J = 7.2$ Hz).

Compound 9 in the reaction scheme above (4.6 g, 21 mmol) was treated with excess of $NaBH_4$ in methanol (40 mL) solution in the presence of $CeCl_3 \cdot 7H_2O$ (155 mg, 0.40 mmol) at 25 °C for 10 min. The reaction was then quenched with 5% HCl solution. The aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with H_2O and sat. NaCl aqueous solution, then dried over $MgSO_4$.

The residue was dissolved in a solution of THF-methanol- H_2O (3:1:1, 20 mL) and treated with $LiOH \cdot H_2O$ (1.0 g, 25 mmol) at 25 °C for 3 h. The reaction mixture was then acidified and extracted with ethyl acetate. The combined organic phase was dried over $MgSO_4$. Concentration and chromatography afforded compound 10 (3.3 g, 82%) as white solid: R_f 0.34 (10:1, CH_2Cl_2 -methanol); 1H NMR (CD_3OD , 300 MHz) δ 7.52 (dd, 1H, $J = 7.6$ Hz, $J = 1.4$ Hz), 7.28 (td, 1H, $J = 7.8$ Hz, $J = 1.5$ Hz), 7.06 (t, 1H, $J = 7.5$ Hz), 6.92 (d, 1H, $J = 8.1$ Hz), 5.33 (q, 1H, $J = 6.6$ Hz), 5.03 (br s, 2H), 4.79 (s, 2H), 1.51 (d, 3H, $J = 7.2$ Hz).

A mixture of hydroxy acid 10 (980 mg, 5.0 mmol), HOBT (743 mg, 5.5 mmol), EDCI (1.05 g, 5.5 mmol), $NaHCO_3$ (1.26 g, 15.0 mmol) and $CH_3NH_2 \cdot HCl$ (371 mg, 5.5 mmol) in DMF (10 mL) was stirred at 25 °C for 23 h. The reaction mixture was diluted with ethyl acetate. The organic solution was washed with H_2O and sat. NaCl solution then dried over $MgSO_4$. Concentration afforded alcohol 11 (664 mg, 64%) as colorless syrup: R_f 0.21 (10:0.5, CH_2Cl_2 -methanol); 1H NMR (CD_3OD , 300 MHz) δ 7.50 (dd, 1H, $J = 7.6$ Hz, $J = 1.6$ Hz), 7.27 (m, 1H), 7.05 (t, 1H, $J = 7.5$ Hz), 6.90 (d, 1H, $J = 8.1$ Hz), 5.34 (q, 1H, $J = 7.2$ Hz), 5.01 (br s, 2H), 4.57 (d, 2H, $J = 3.0$ Hz), 2.85 (s, 3H), 1.54 (d, 3H, $J = 7.0$ Hz).

EXAMPLE 381

[2-(1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl)phenoxy]-N-methylacetamide

DEAD (352 μ L, 2.2 mmol) was added dropwise to a solution of alcohol 11 (312 mg, 1.5 mmol), Triphenylphosphine (586 mg, 2.2 mmol) and sulfonamide 3 (452 mg, 1.5 mmol) in THF (6 mL) at 25 °C under Ar. The mixture was stirred at 25 °C for 22 h, then concentrated in vacuo. Small amount of crude product was purified by HPLC to afford the compound (34 mg) as white foam: R_f 0.35 (10:10, hexane-ethyl acetate); 1H NMR ($CDCl_3$, 300 MHz) δ 7.95 (m, 1H), 7.68 (br s, 2H), 7.44 (br s, 2H), 7.26

(br s, 1H), 6.24-6.95 (m, 6H), 6.32 (q, 1H, $J = 7.2$ Hz), 4.69 (m, 1H), 4.52 (m, 1H), 2.95 (s, 3H), 1.50 (d, 3H, $J = 7.2$ Hz); LCMS 3.46 min, m/z 517.1 ($M+Na^+$, $C_{23}H_{21}ClF_2N_2O_4S$ requires 494.94).

5 A mixture of hydroxy acid 10 (980 mg, 5.0 mmol), HOBT (743 mg, 5.5 mmol), EDCI (1.05 g, 5.5 mmol), $NaHCO_3$ (1.26 g, 15 mmol) and $CH_3ONH_2 \cdot HCl$ (459 mg, 5.5 mmol) in DMF (20 mL) was stirred at 25 °C for 23 h. The reaction mixture was diluted with ethyl acetate. The organic solution was washed with H_2O and sat. NaCl solution then dried over $MgSO_4$. Concentration afforded the desired product (340 mg, 30%) as colorless syrup: R_f 0.19 (10:0.5, CH_2Cl_2 -methanol); 1H NMR ($CDCl_3$, 300 MHz) δ 7.44 (d, 1H, $J = 7.8$ Hz), 7.24 (t, 1H, $J = 7.2$ Hz), 7.00 (t, 1H, $J = 7.4$ Hz), 6.88 (d, 1H, $J = 8.1$ Hz), 5.23 (m, 1H), 4.90 (s, 2H), 4.57 (d, 2H, $J = 2.7$ Hz), 3.70 (s, 3H), 1.48 (d, 3H, $J = 6.6$ Hz).

EXAMPLE 382

[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]-N-methoxyacetamide

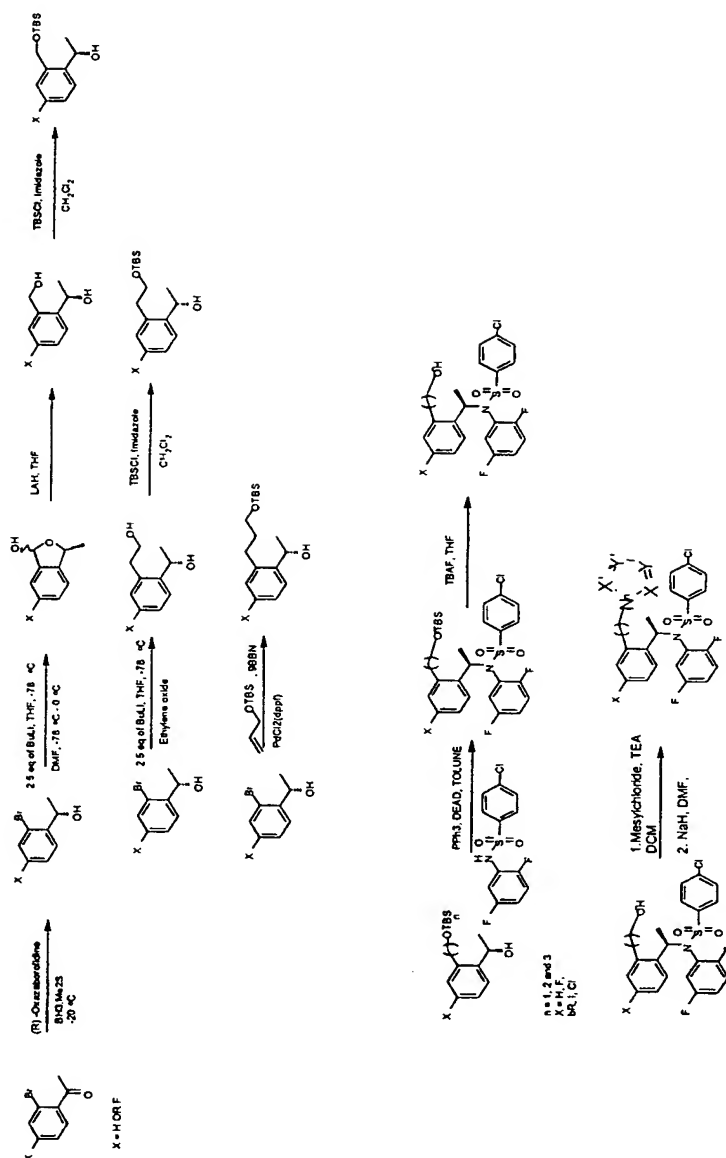
15 DEAD (357 μ L, 2.3 mmol) was added dropwise to a solution of alcohol 12 (340 mg, 1.5 mmol), Triphenylphosphine (595 mg, 2.3 mmol) and sulfonamide 3 (458 mg, 1.5 mmol) in THF (6 mL) at 25 °C under Ar. The mixture was stirred at 25 °C for 22 h, then concentrated in vacuo. Crude product was purified by HPLC to afford the desired product (144 mg) as white foam: R_f 0.38 (10:10, hexane-ethyl acetate); 1H NMR ($CDCl_3$, 300 MHz) δ 10.81 (m, 1H), 7.72 (m, 2H), 7.47 (m, 2H), 7.27 (m, 1H), 6.24-6.97 (m, 7H), 4.80 (m, 1H), 4.60 (m, 1H), 3.88 (s, 3H), 1.48 (d, 3H, $J = 6.9$ Hz); LCMS 3.19 min, m/z 533 ($M+Na^+$, $C_{23}H_{21}ClF_2N_2O_5S$ requires 510.94).

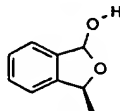
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EXAMPLE 383

Numerous compounds according to the present invention can be prepared employing the general scheme set forth in SCHEME 383.

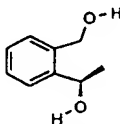
SCHEME 383



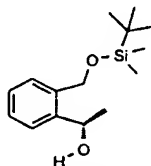
EXAMPLE 384

$R_f = 0.25$ (3:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.46-7.21 (m, 4H), 6.51-6.40 (dd, 1H), 5.52 (dq, 1H), 2.93-2.89 (m, 1H), 1.60-1.33 (dd, 3H).

5

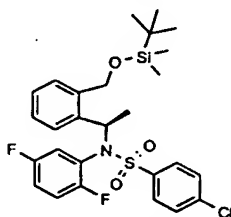
EXAMPLE 385

$R_f = 0.23$ (2:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.66-7.16 (m, 4H), 5.16 (q, 1H), 4.87-4.60 (dd, 2H), 3.13 (b, 2H), 1.59 (d, 3H).

EXAMPLE 386

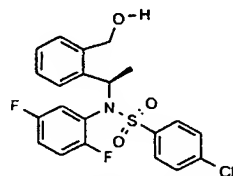
10

$R_f = 0.25$ (15:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.43-7.14 (m, 4H), 5.06 (m, 1H), 4.86-4.56 (dd, 2H), 3.07 (s, 3.07), 1.48 (d, 3H), 0.85 (s, 9H), 0.00 (m, 6H).

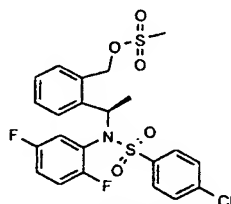
EXAMPLE 387

15

$R_f = 0.30$ (20:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.64-6.22 (m, 11H), 5.87 (q, 1H), 5.10 (m, 1H), 4.84 (m, 1H), 1.50 (m, 3H), 0.97 (s, 9H), 0.10 (d, 6H).

EXAMPLE 388

$R_f = 0.25$ (3:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ : 7.63-7.72 (m, 11H), 6.02 (b, 1H), 5.01-4.85 (m, 2H), 2.53-2.16 (bb, 1H), 1.49-1.38 (m, 3H).

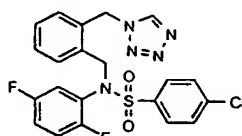
EXAMPLE 389

$R_f = 0.25$ (3:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ : 7.69-6.75 (m, 11H), 5.89 (m, 2H), 5.42-5.30 (m, 1H), 3.09 (s, 3H), 1.51-1.39 (m, 3H).

10

EXAMPLE 390

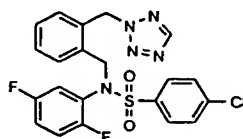
4-chloro-N-(2,5-difluorophenyl)-N-[2-(1H-tetrazol-1-ylmethyl)benzyl]benzenesulfonamide



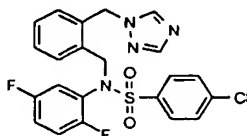
$R_f = 0.48$ (1:1; ethyl acetate:hexanes). ^1H NMR (CDCl_3) δ (ppm): 8.96 (s, 1H), 7.76-7.74 (d, 2H), 7.60-7.58 (d, 2H), 7.35-7.09 (m, 3H), 6.99-6.90 (m, 3H), 6.75-6.69 (m, 1H), 5.93 (s, 2H), 4.82 (s, 2H). LC-MS calculated for $\text{C}_{21}\text{H}_{16}\text{ClF}_2\text{N}_5\text{O}_2\text{S}$ 476; Observed: 476.

EXAMPLE 391

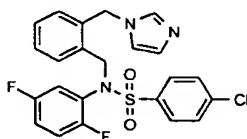
4-chloro-N-(2,5-difluorophenyl)-N-[2-(2H-tetrazol-2-ylmethyl)benzyl]benzenesulfonamide



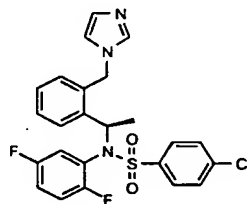
$R_f = 0.50$ (2:1; hexanes: ethyl acetate). (ppm): 8.515 (s, 1H), 7.76-7.72 (m, 2H), 7.54-7.51 (m, 2H), 7.23-6.69 (m, 7H), 6.08 (s, 2H), 4.93 (s, 2H). LC-MS calculated for $\text{C}_{21}\text{H}_{16}\text{ClF}_2\text{N}_5\text{O}_2\text{S}$: 476; Observed: 476.

EXAMPLE 392**4-chloro-N-(2,5-difluorophenyl)-N-[2-(1H-1,2,4-triazol-1-ylmethyl)benzyl]benzenesulfonamide**Mp = 147-148 (ethyl acetate/hexanes). R_f = 0.28 (19:1; DCM:methanol). ^1H NMR δ (ppm):

5 8.26 (s, 1H), 8.08 (s, 1H), 7.71-7.68 (m, 2H), 7.54-7.51 (m, 2H), 7.25-6.71 (m, 7H), 5.60 9s, 2H, 4.80 (s, 2H). LC-MS calculated for $\text{C}_{22}\text{H}_{17}\text{ClF}_2\text{N}_4\text{O}_2\text{S}$: 475. Observed: 475.

EXAMPLE 393**4-chloro-N-(2,5-difluorophenyl)-N-[2-(1H-imidazol-1-ylmethyl)benzyl]benzenesulfonamide**Mp = 166-167 (DCM/hexanes). R_f = 0.31 (19:1; DCM:methanol). ^1H NMR δ (ppm):

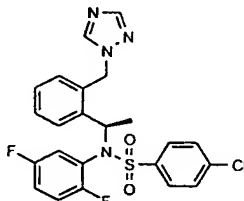
10 7.65-7.50 (m, 5H), 7.33-7.07 (m, 3H), 6.99-6.87 (m, 4H), 6.72-6.71 (m, 1H), 5.40 (s, 2H), 4.69 (s, 2H). LC-MS calculated for $\text{C}_{23}\text{H}_{18}\text{ClF}_2\text{N}_3\text{O}_2\text{S}$: 474. Observed 474.

EXAMPLE 394**4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-[2-(1H-imidazol-1-ylmethyl)phenyl]ethyl]benzenesulfonamide hydrochloride**

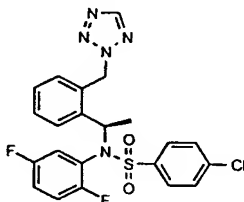
15 R_f = 0.50 (10:1; DCM:methanol). ^1H NMR (CD_3OD) δ (ppm): 7.77-7.75 (m, 2H), 7.63-7.52 (m, 3H), 7.30-6.80 (8.5H), 6.55 (m, 0.5H), 5.88-5.81 (m, 2H), 5.49-5.34 (m, 1H), 1.46-1.26 (m, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{20}\text{ClF}_2\text{N}_3\text{O}_2\text{S}$: 487. Observed 488 (MH+).

EXAMPLE 395

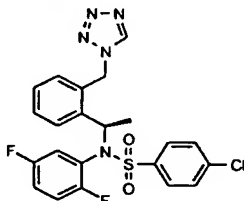
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(1H-1,2,4-triazol-1-ylmethyl)phenyl]ethyl)benzenesulfonamide



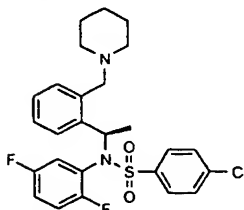
- 5 $R_f = 0.25$ (97:3; DCM; methanol). $^1\text{H NMR}$ (CD_3OD) δ (ppm): 8.26 (s, 1H), 8.00 (s, 1H), 7.70-6.41 (m, 13H), 6.09-5.91 (m, 2H), 5.44 (d, 1H), 1.42-1.25 (dd 3H). LC-MS calculated for $\text{C}_{23}\text{H}_{19}\text{ClF}_2\text{N}_4\text{O}_2\text{S}$: 488. Observed 489 (MH $^+$).

EXAMPLE 396

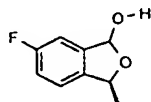
- 10 $R_f = 0.34$ (6:1; hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 8.53 (s, 1H), 7.74-6.59 (m, 13H), 6.29-6.22 (m, 1H), 5.84 (d, 1H), 1.42-1.25 (dd, 3H). LC-MS calculated for $\text{C}_{22}\text{H}_{18}\text{ClF}_2\text{N}_5\text{O}_2\text{S}$: 489. Observed 490 (MH $^+$).

EXAMPLE 397

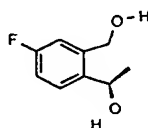
- 15 $R_f = 0.25$ (2:1; hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 8.34 (s, 1H), 7.72-7.69 (m, 2H), 7.53-6.35 (m, 10H), 6.37 (d, 1H), 5.91 (q, 1H), 5.74 (d, 1H), 1.40-1.24 (dd, 3H). LC-MS calculated for $\text{C}_{22}\text{H}_{18}\text{ClF}_2\text{N}_5\text{O}_2\text{S}$: 489. Observed 490 (MH $^+$).

EXAMPLE 398

$R_f = 0.50$ (10:1 DCM:methanol). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.66-6.82 (m, 11H), 6.14 (br, 1H),
 5 3.30-3.14 (m, 6H), 1.83-1.48 (m, 9H). LC-MS calculated for $\text{C}_{26}\text{H}_{27}\text{ClF}_2\text{N}_2\text{O}_2\text{S}$: 504. Observed 505
 (MH $^+$).

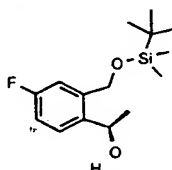
EXAMPLE 399

$R_f = 0.25$ (3:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.18-7.06 (m, 3H), 6.37
 10 (d, 1H), 5.23 (q, 1H), 3.01 (d, 1H), 1.58 (t, 3H).

EXAMPLE 400

$R_f = 0.23$ (2:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.46-7.41 (m, 1H), 7.08-
 6.98 (m, 2H), 5.10 (q, 1H), 4.80-4.59 (dd, 2H), 3.08 (s, 1H), 3.93 (s, 1H), 1.53 (d, 3H).

15

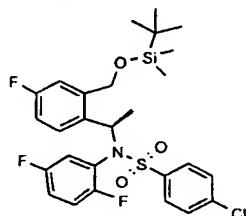
EXAMPLE 401

$R_f = 0.25$ (15:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.37-7.31 (m, 1H), 6.99-
 6.82 (m, 2H), 4.97 (q, 1H), 4.79-4.52 (dd, 2H), 2.76 (b, 1H), 1.39 (d, 3H), 0.79 (s, 9H), 0.00 (d, 6H).

WO 00/50391

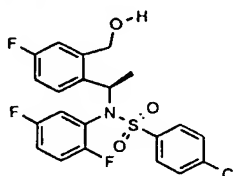
210

PCT/US00/04560

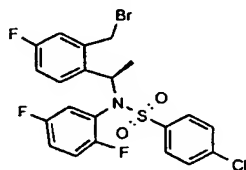
EXAMPLE 402

$R_f = 0.30$ (20:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.63-6.16 (m, 10H), 5.58 (q, 1H), 4.79 (m, 2H), 1.36 (m, 3H), 0.79 (s, 9H), -0.06 (d, 6H).

5

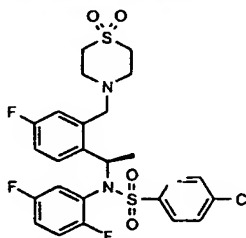
EXAMPLE 403

$R_f = 0.25$ (3:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.66-7.27 (m, 4H), 7.03-6.47 (m, 6H), 5.94 (d, 1H), 4.94 (m, 2H), 2.56-2.26 (bb, 1H), 1.50-1.40 (m, 3H).

EXAMPLE 404

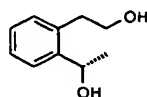
10

$R_f = 0.30$ (15:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.72-7.41 (m, 4H), 7.10-6.42 (m, 6H), 5.93 (m, 1H), 5.29-5.10 (m, 1H), 4.47-4.39 (m, 1H), 1.48-1.23 (m, 3H).

EXAMPLE 405

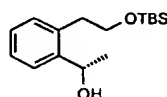
15

$R_f = 0.19$ (3:1; hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.66-7.74 (m, 2H), 7.56-7.40 (m, 2H), 7.06-6.37 (m, 6H), 6.44-6.37 (m, 1H), 4.49 (d overlaps d, 1H), 3.52 (d, 1H), 3.18-3.03 (m, 8H), 1.44 (d, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{24}\text{ClF}_3\text{N}_2\text{O}_4\text{S}_2$: 572. Observed 572.

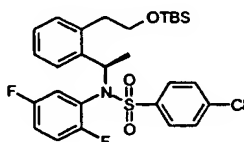
EXAMPLE 406

A solution of n-BuLi in THF (2.5 M, 17.6 mL, 44 mmol) was added dropwise within 30 min to a solution of (s)-(-)-2-bromo- α -methylbenzyl alcohol (3.9 g, 19.4 mmol) in THF at -78°C under Ar.

5 After having been stirred for 40 min, the generated suspension was warmed to 0°C , and ethylene oxide (5 mL, 100 mmol) was added. The mixture was stirred at 0°C for 1 h. The reaction was quenched with 1 N HCl aqueous solution. The aqueous phase was extracted with ethyl acetate. The combined organic solution was washed with water and sat. NaCl solution, then dried over Na_2SO_4 . Concentration and flush column chromatography afforded the diol (1.4 g, 44%) as colorless liquid: R_f 0.16 (10:10, hexanes:ethyl acetate); ^1H NMR (CDCl_3 , 300 MHz) δ 7.50 (m, 1H), 7.25 (m, 2H), 7.17 (m, 1H), 5.13 (q, 1H, $J = 6.6$ Hz), 3.90 (m, 1H), 3.76 (m, 1H), 3.00 (m, 1H), 2.86 (m, 1H), 2.94 (br s, 1H), 1.52 (d, 3H, $J = 6.6$ Hz).

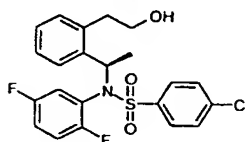
EXAMPLE 407

15 A solution of the diol prepared according to the previous example (890 mg, 5.4 mmol) in CH_2Cl_2 (21 mL) was treated with TBSCl (848 mg, 5.6 mmol) in the presence of imidazole (803 mg, 11.8 mmol) at 25°C under Ar for 40 min. The reaction was quenched with H_2O . The aqueous phase was extracted with CH_2Cl_2 . The combined organic phase was dried over Na_2SO_4 . Concentration afforded product (1.5 g, 100%) as colorless liquid: R_f 0.21 (10:1, hexanes:ethyl acetate); ^1H NMR (CDCl_3 , 300 MHz) δ : 7.50 (m, 1H), 7.27 (m, 2H), 7.22 (m, 1H), 5.18 (m, q, 1H, $J = 6.3$ Hz), 3.94 (m, 20 1H), 3.87 (m, 1H), 3.28 (m, 1H), 3.01 (m, 2H), 1.56 (d, 3H, $J = 6.3$ Hz), 0.85 (s, 9H), 0.00 (s, 6H).

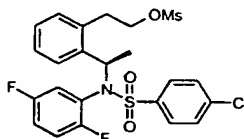
EXAMPLE 408

25 To a solution of the alcohol prepared according to the previous example (4.4 g, 16 mmol) in toluene (53 mL) at 25°C under Ar, were added triphenylphosphine (5.4 g, 20.5 mmol) and sulfonamide 3 (5.3g, 17.4 mmol). The mixture was cooled to 0°C , and DEAD (3.0 mL, 19 mmol) was added dropwise. After the addition, the mixture was stirred at 25°C for 36 h. Concentration and chromatography afforded product 4 (6.66 g, 75%) as colorless syrup: R_f 0.39 (10:1, hexanes:ethyl acetate); ^1H NMR (CDCl_3 , 300 MHz) δ : 7.62 (m, 2H), 7.38 (m, 2H), 7.16 (m, 2H), 6.29-7.07 (m, 5H),

5.94 (m, 1H), 3.86 (m, 2H), 3.26 (m, 1H), 2.79 (m, 1H), 1.53 (m, 3H), 0.88 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H).

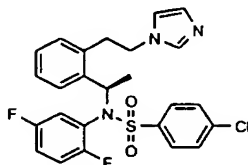
EXAMPLE 409

5 A solution of product prepared according to the previous example (6.6 g, 11.7 mmol) in THF (55 mL) was treated with TBAF solution (1.0 M in THF, 12 mL, 12.2 mmol) at 25 °C under Ar for 40 min. The reaction was quenched with H₂O. The aqueous phase was extracted with ethyl acetate and the combined organic solution was washed with sat. NaCl aqueous solution, then dried over MgSO₄. Concentration and chromatography afforded 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(2-hydroxyethyl)phenyl]ethyl)benzenesulfonamide (4.8 g, 92%) as colorless gum: R_f 0.28 (10:4, hexanes:ethyl acetate); ¹H NMR (CDCl₃, 300 MHz) δ 7.62 (m, 2H), 7.43 (m, 2H), 7.19 (m, 2H), 6.40-7.00 (m, 5H), 5.99 (m, 1H), 3.95 (t, 2H, J = 6.6 Hz), 3.34 (m, 1H), 3.00 (m, 1H), 1.92 (s, 1H), 1.48 (m, 3H); LCMS 3.36 min, *m/z* 469.0 (M+H⁺+H₂O, C₂₂H₂₀ClF₂NO₃S requires 451.91).

EXAMPLE 410

15 A solution of 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(2-hydroxyethyl)phenyl]ethyl)benzenesulfonamide (422 mg, 0.94 mmol) in triethylamine (5.0 mL) was treated with MsCl (109 μL, 1.4 mmol) at 0 °C under Ar for 3 h. The reaction mixture was diluted with ethyl acetate. The organic solution was washed with H₂O and sat. NaCl aqueous solution, then dried over MgSO₄. Concentration in vacuo afforded the mesylate (450 mg, 91%) as light yellow syrup: R_f 0.25 (10:4, hexanes:ethyl acetate).

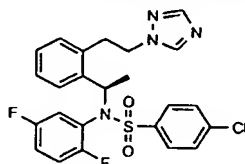
25 A solution of 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(2-hydroxyethyl)phenyl]ethyl)benzenesulfonamide (422 mg, 0.94 mmol) in triethylamine (5.0 mL) was treated with MsCl (109 μL, 1.4 mmol) at 0 °C under Ar for 3 h. The reaction mixture was diluted with ethyl acetate. The organic solution was washed with H₂O and sat. NaCl aqueous solution, then dried over MgSO₄. Concentration in vacuo afforded mesylate (450 mg, 91%) as light yellow syrup: R_f 0.25 (10:4, hexanes:ethyl acetate).

EXAMPLE 411

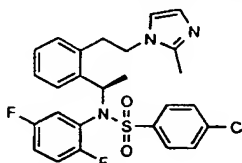
Imidazole (82 mg, 1.2 mmol) was added slowly to a suspension of NaH (60%, 58 mg, 1.4 mmol) in DMF (2.0 mL) at 25 °C under Ar. After having been stirred at 25 °C for 20 min, the generated solution was added to a solution of mesylate 5 (420 mg, 0.80 mmol) in THF (6.0 mL). The mixture was stirred at 25 °C overnight. The reaction was quenched with H₂O and the aqueous phase was extracted with ethyl acetate. The dried organic solution was concentrated in vacuo. Chromatography afforded 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride as colorless syrup (211 mg, 53%) as colorless gum: R_f 0.31 (10:0.5 CH₂Cl₂-methanol); ¹H NMR (CDCl₃, 300 MHz) δ 7.40-7.66 (m, 5H), 6.22-7.30 (m, 9H), 5.62 (m, 1H), 4.42 (m, 1H), 4.18 (m, 1H), 3.61 (m, 1H), 3.22 (m, 1H), 1.34 (d, 3H, J = 6.3Hz); LCMS calculated for C₂₅H₂₂ClF₂N₃O₂S 502. Observed: 502.

EXAMPLE 412**4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride**

A solution of HCl in Et₂O (1.0 M, 398 μL, 0.40 mmol) was added dropwise to a solution of 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride (100 mg, 0.20 mmol) in CH₂Cl₂ (2.0 mL) at 25 °C under Ar. After having been stirred for 30 min, the solvents were removed in vacuo. The residue was purified by chromatography to afford 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride (99 mg, 92%) as white solid. m.p. 205.0–206.0 °C; R_f 0.32 (10:0.5, CH₂Cl₂-methanol); ¹H NMR (CD₃OD, 300 MHz) δ 9.22 (s, 1H), 7.76-8.07 (m, 6H), 6.57-7.52 (m, 7H), 6.23 (m, 1H), 4.93 (m, 2H), 3.91 (m, 1H), 3.78 (m, 1H), 1.69 (d, 3H, J = 6.9 Hz); LCMS 3.04 min, m/z 502.05 (M+H⁺-HCl, C₂₅H₂₂ClF₂N₃O₂S·HCl requires 501.9836.46).

EXAMPLE 413**4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-1,2,4-triazol-1-yl)ethyl]phenyl} ethyl) benzenesulfonamide**

1, 2, 4-Triazole (101 mg, 1.5 mmol) was treated with NaH (60%, 70 mg, 1.8 mmol) in THF (7.0 mL) and DMF (0.5 mL) at 25 °C under Ar for 30 min. The generated suspension was added slowly to a solution of mesylate 5 (0.97 mmol) in THF (3.0 mL) and the mixture was stirred for 48 h. The reaction was quenched with H₂O and the aqueous phase was extracted with ethyl acetate. The dried organic solution was concentrated and chromatography afforded 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-1,2,4-triazol-1-yl)ethyl]phenyl} ethyl) benzenesulfonamide (260 mg, 53%) as white crystal: m.p. 116-118 °C; R_f 0.28 (10:10, hexanes:ethyl acetate); ¹H NMR (CDCl₃, 300 MHz) δ 8.01 (br s, 2H), 7.39-7.3 (m, 4H), 6.32-7.11 (m, 7H), 5.83 (m, 1H), 4.65 (m, 1H), 4.89 (m, 1H), 3.29-3.68 (m, 2H), 1.35 (m, 3H); LCMS 3.43 min, *m/z* 503.05 (M+H⁺, C₂₄H₂₁ClF₂N₄O₂S requires 502.96).

EXAMPLE 414**4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(2-methyl-1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride**

2-Methylimidazole (77 mg, 0.94 mmol) was treated with NaH (60%, 27 mg, 1.1 mmol) in DMF (1.0 mL) at 25 °C under Ar for 30 min. The generated solution was added slowly to a solution of mesylate 5 (250 mg, 0.47 mmol) in THF and the mixture was stirred at 25 °C for 26 h. The reaction was quenched with H₂O and the aqueous phase was extracted with ethyl acetate. The dried organic solution was concentrated in vacuo. Chromatography afforded the desired product (39 mg, 16%) as a colorless gum: R_f 0.28 (10:0.5, CH₂Cl₂-methanol); ¹H NMR (CDCl₃, 300 MHz) δ 7.60 (m, 2H), 7.42 (m, 2H), 7.15 (m, 2H), 6.20-6.98 (m, &H), 5.52 (m, 1H), 4.30 (m, 1H), 4.06 (m, 1H), 3.69 (m, 1H), 3.12 (m, 1H), 2.10 (m, 3H), 1.27 (m, 3H); LCMS 3.07 min, *m/z* 516.10 (M+H⁺, C₂₆H₂₄ClF₂N₃O₂S requires 516.00).

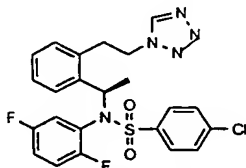
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(2-methyl-1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide (39 mg, 0.075 mmol) was dissolved in CH₂Cl₂ (2.0 mL) and treated with HCl – Et₂O solution (1.0 M, 83 μL) at 25 °C for 15 min. Solvents were removed in vacuo

and chromatography afforded 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(2-methyl-1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride (26 mg, 61%) as white solid: m.p. 190.5-192.0 °C; R_f 0.38 (10:1, CH_2Cl_2 -methanol); ^1H NMR (CD_3OD , 300 MHz) δ 7.39-7.67 (m, 5H), 7.29 (m, 1H), 6.18-7.12 (m, 7H), 5.67 (q, 1H, $J = 6.9$ Hz), 4.44 (m, 1H), 4.35 (m, 1H), 3.59 (m, 1H), 3.25 (m, 1H), 2.27 (m, 3H), 1.31 (d, 3H, $J = 6.6$ Hz); LCMS 3.07 min, m/z 516.05 ($\text{M}+\text{H}^+-\text{HCl}$, $\text{C}_{26}\text{H}_{24}\text{ClF}_2\text{N}_3\text{O}_2\text{SHCl}$ requires 516.00).

The following compounds were prepared using the preparative schemes described in the previous Examples.

EXAMPLE 415

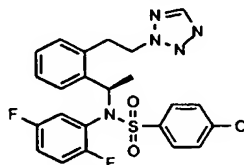
10 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-tetraazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide



15 R_f 0.16 (10:5, hexanes:ethyl acetate); ^1H NMR (CDCl_3 , 300 MHz) δ 8.75 (s, 1H), 7.42-7.74 (m, 4H), 6.30-7.20 (m, 7H), 5.94 (m, 1H), 4.98 (m, 1H), 4.75 (m, 1H), 3.56 (m, 2H), 1.40 (d, 3H, $J = 6.9$ Hz); LCMS 3.56 min, m/z 504.05 ($\text{M}+\text{H}^+$, $\text{C}_{23}\text{H}_{20}\text{ClF}_2\text{N}_5\text{O}_2\text{S}$ requires 503.95).

EXAMPLE 416

 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(2H-tetraazol-2-yl)ethyl]phenyl}ethyl)benzenesulfonamide

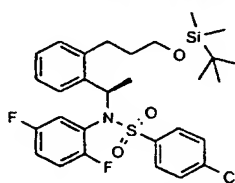


20 R_f 0.40 (10:4, hexanes:ethyl acetate); ^1H NMR (CDCl_3 , 300 MHz) δ 8.55 (s, 1 H), 7.63 (m, 2H), 7.41 (m, 2H), 6.45-7.14 (m, 7H), 5.88 (m, 1H), 5.01 (m, 2H), 3.80 (m, 1H), 3.52 (m, 1H), 1.45 (m, 3H); LCMS 4.37 min, m/z 526.05 ($\text{M}+\text{Na}^+$, $\text{C}_{23}\text{H}_{20}\text{ClF}_2\text{N}_5\text{O}_2\text{S}$ requires 503.95).

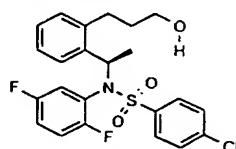
WO 00/50391

216

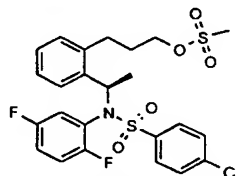
PCT/US00/04560

EXAMPLE 417

$R_f = 0.25$ (15:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.45-6.61 (m, 11H), 5.78 (q, 1H), 3.65-3.52 (m, 2H), 3.00 (m, 1H), 2.66-2.55 (m, 1H), 1.79-1.59 (m, 2H), 1.43-1.30 (m, 3H), 0.84 (d, 9H), 0.01 (d, 6H).

EXAMPLE 418

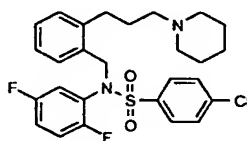
$R_f = 0.23$ (3:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.66-7.60 (m, 2H), 7.42-7.40 (m, 2H), 7.19-6.59 (m, 7H), 5.94 (q, 1H), 3.83-3.76 (m, 2H), 3.21-3.11 (m, 1H), 2.87-2.77 (m, 1H), 2.01-1.88 (m, 2H), 1.72 (t, 1H), 1.53 (m, 3H).

EXAMPLE 419

$R_f = 0.30$ (3:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.65 (m, 2H), 7.42 (m, 2H), 7.18-6.29 (m, 7H), 6.93 (m, 1H), 4.36 (m, 2H), 3.24 (m, 1H), 3.10 (s, 3H), 2.87 (m, 1H), 2.14 (m, 2H), 1.53 (m, 3H).

EXAMPLE 420

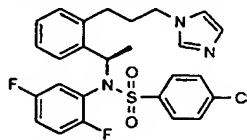
4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-piperidinyl)propyl]benzyl}benzenesulfonamide



$R_f = 0.25$ (9:1;DCM:methanol). $^1\text{H NMR}$ (CD_3OD) δ (ppm): 7.75-7.62 (m, 4H), 7.19-6.89 (m, 7H), 4.76 (s, overlaps HOD, 2H), 2.95-2.85 (m, 8H), 2.11-1.95 (m, 2H), 1.81-1.75 (m, 4H), 1.65-1.55 (m, 2H). LC-MS calculated for $\text{C}_{27}\text{H}_{30}\text{ClF}_2\text{N}_2\text{O}_2\text{S}$: 519. Observed 519 (M^+).

EXAMPLE 421

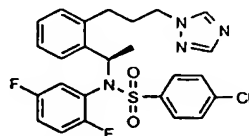
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride



5 $R_f = 0.34$ (19:1;DCM:methanol). $^1\text{H NMR}$ (CD_3OD) δ (ppm): 7.74 (s, 1H), 7.70-7.57 (m, 4H), 7.24 (s, 1H), 7.22-6.61 (m, 8.5H), 6.3 (br m, 0.5H), 5.87 (q, 1H), 4.19 (t, 2H), 3.02-2.81 (m, 2H), 2.21-2.11 (m, 2H), 1.51-1.49 (m, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{24}\text{ClF}_2\text{N}_3\text{O}_2\text{S}$: 516. Observed 516 (M^+).

EXAMPLE 422

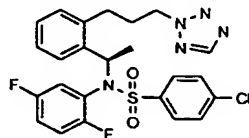
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-1,2,4-triazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide



10 $R_f = 0.29$ (19:1;DCM:methanol). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 8.19 (s, 1H), 8.00 9s, 1H), 7.67-6.30 (m, 11H), 5.92 (q, 1H), 4.36 (t, 2H), 3.17-3.07 (m, 1H), 2.91-2.82(m, 1H), 2.38-2.22(m, 2H), 1.49 (br, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{23}\text{ClF}_2\text{N}_4\text{O}_2\text{S}$: 517. Observed 517 (M^+).

EXAMPLE 423

4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(2H-tetraazol-2-yl)propyl]phenyl}ethyl)benzenesulfonamide

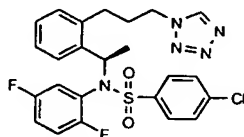


15 $R_f = 0.50$ (3:1 hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 8.81 (Ss, 1H), 7.69-6.24 (m, 11), 5.93 (q, 1H), 4.65 (t, 2H), 3.15-2.85 (m, 2H), 2.55-2.25 (m, 2H), 1.31(d, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{22}\text{ClF}_2\text{N}_5\text{O}_2\text{S}$: 518. Observed 215 ($\text{M}^+ - 303$).

20

EXAMPLE 424

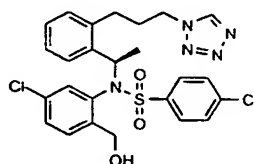
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-tetrazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.20$ (2:1 hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 9.23 (s, 1H), 7.70-6.27 (m, 11H), 5.92 (q, 1H), 4.65 (t, 2H), 3.20-2.90 (m, 2H), 2.54-2.33 (m, 2H), 1.46 (d, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{22}\text{ClF}_2\text{N}_5\text{O}_2\text{S}$: 518. Observed 518 (M^+).

EXAMPLE 425

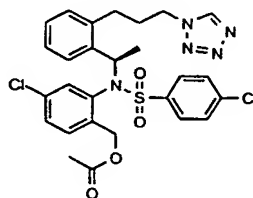
4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.29$ (19:1 DCM:methanol). ^1H NMR (CDCl_3) δ (ppm): 7.74-(6.57 (m, 13H), 6.28-6.19 (m, 1H), 6.01-5.94 (m, 1H), 0004.19-4.03 (m, 2H), 3.86-3.75 (m, 1H), 3.42-3.16 (m, 2H), 2.93-2.83 (m, 1H), 2.28-1.98 (m, 4H), 1.39 (d, 3H). LC-MS calculated for $\text{C}_{27}\text{H}_{27}\text{Cl}_2\text{N}_3\text{O}_3\text{S}$: 544.5. Observed: 544.5 (M^+).

EXAMPLE 426

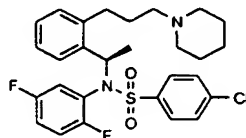
4-chloro-2-[[[(4-chlorophenyl)sulfonyl]((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)amino]benzyl acetate



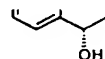
$R_f = 0.26$ (19:1 DCM:methanol). ^1H NMR (CDCl_3) δ (ppm): 7.68-6.76 (m, 14H), 6.23 (d, 1H), 5.97 (q, 1H), 4.36 (d, 1H), 4.15 (t, 2H), 3.58 (d, 1H), 3.18-3.09 (m, 1H), 2.97-2.88 (m, 1H), 2.34-2.21 (m, 2H), 1.89 (s, 3H), 1.43 (d, 3H).

EXAMPLE 427

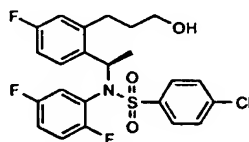
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1-piperidinyl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride



$R_f = 0.68$ (9:1 DCM:methanol). ^1H NMR (CD_3OD) δ (ppm): 7.57-7.28 (m, 5H), 7.09-6.93 (m, 3H), 6.68-6.10 (m, 3H), 5.74 (q, 1H), 3.87-2.58 (m, 8H), 0.198-1.85 (m, 2H), 1.71-1.61 (m, 4H), 1.49-1.16 (m, 5H). LC-MS calculated for $\text{C}_{28}\text{H}_{31}\text{ClF}_2\text{N}_2\text{O}_2\text{S}$: 533. Observed: 533 (M^+).

EXAMPLE 428

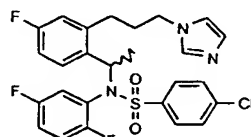
A solution of 9-BBN in THF (0.5 M, 91 mL, 45 mmol) was added dropwise to a solution of allyloxy-*tert*-butyldimethylsilane (8.7 g, 50 mmol) in THF (25 mL) at 0°C under Ar. The mixture was stirred at 0°C for 1 h, then at 60°C for additional 1 h. the solution was then cooled to 25°C . To the generated solution at 25°C , were added compound 19 (8.85 g, 40 mmol), $\text{PdCl}_2(\text{dppf})$ (990 mg, 1.2 mmol) and 3 M NaOH aqueous solution (13.5 mL, 40.4 mmol). The mixture was refluxed at 60°C for 12 h. The solution was extracted with CH_2Cl_2 and the combined organic solution was washed with sat. NH_4Cl solution and sat. NaCl solution, then dried over MgSO_4 . Chromatography afforded the desired product (21) (11.4 g, 90%) as colorless syrup: R_f 0.12 (10:1, hexanes:ethyl acetate); ^1H NMR (CDCl_3 , 300 MHz) δ 7.41 (m, 1H), 7.69 (m, 2H), 5.09 (m, 1H), 3.58 (m, 2H), 2.66 (m, 2H), 2.11 (s, 1H), 1.73 (m, 2H), 1.39 (m, 3H), 0.84 (s, 9H), -0.01 (s, 3H), -0.02 (s, 3H).

EXAMPLE 429

R_f 0.30 (10:5, hexanes:ethyl acetate); ^1H NMR (CDCl_3 , 300 MHz) δ 7.65 (m, 2H), 7.42 (d, 2H), 7.00 (m, 2H), 6.91 (m, 1H), 6.33-6.74 (m, 3H), 5.92 (q, 1H, $J = 6.6$ Hz), 3.79 (s, 2H), 3.15 (m, 1H), 2.82 (m, 1H), 2.68 (s, 1H), 1.92 (m, 2H), 1.51 (m, 3H); LCMS 3.55 min, m/z 501.15 ($\text{M}^+ + \text{H}_2\text{O}$, $\text{C}_{23}\text{H}_{21}\text{ClF}_3\text{NO}_3\text{S}$ requires 483.94).

EXAMPLE 430

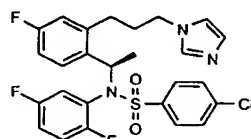
4-chloro-N-(2,5-difluorophenyl)-N-(1-{4-fluoro-2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride



$R_f = 0.44$ (10:1;DCM:methanol). ^1H NMR (CD_3OD) δ (ppm): 7.93-6.37 (m, 13H), 5.89 (m, 1H), 4.16 (t, 2H), 3.10-2.85 (m, 2H), 2.31-2.17 (m, 2H), 1.52-1.50 (m, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{23}\text{ClF}_3\text{N}_3\text{O}_2\text{S}$: 534. Observed 534 (M^+).

EXAMPLE 431

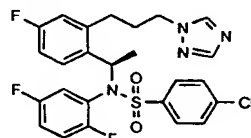
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride



$R_f = 0.38$ (19:1;DCM:methanol). ^1H NMR (CDCl_3) δ (ppm): 9.64 (s, 0.4H), 9.56 (s, 0.6H), 7.71-7.40 (m, 6H), 7.02-6.20 (m, 6H), 5.92 (q, 1H), 4.62-4.47 (m, 2H), 3.15-2.95 (m, 2H), 2.57-2.22 (m, 2H), 1.41 (d, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{23}\text{ClF}_3\text{N}_3\text{O}_2\text{S}$: 534. Observed 534 (M^+).

EXAMPLE 432

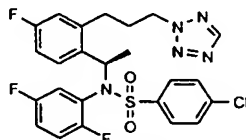
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1H-1,2,4-triazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.38$ (1:1 hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 8.19 (s, 1H), 8.01 (s, 1H), 7.67-7.45 (m, 4H), 6.70-6.28 (m, 6H), 5.87 (q, 1H), 4.34 (t, 2H), 3.11-2.98 (m, 1H), 2.91-2.80 (m, 1H), 2.38-2.22 (m, 2H), 1.46 (d, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{22}\text{ClF}_3\text{N}_4\text{O}_2\text{S}$: 535. Observed 535 (M^+).

EXAMPLE 433

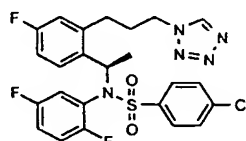
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(2H-tetraazol-2-yl)propyl]phenyl}ethyl)benzenesulfonamide



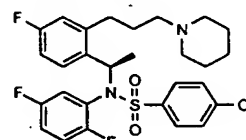
5 $R_f = 0.33$ (3:1 hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 8.58 (s, 1H), 7.66-7.32 (m, 4H), 7.01-6.31 (m, 6H), 5.84 (q, 1H), 4.83 (dt, 2H), 3.17-3.07 (m, 1H), 2.88-2.78 (m, 1H), 2.43 (p, 2H), 1.52 (d, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{21}\text{ClF}_3\text{N}_5\text{O}_2\text{S}$: 536. Observed 233 ($\text{M}^+ - 303$).

EXAMPLE 434

4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1H-tetraazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide



10 $R_f = 0.50$ (1:1 hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 8.79 (s, 1H), 7.69-7.46 (m, 4H), 7.02-6.23 (m, 6H), 5.92-5.84 (m, 1H), 4.66 (t, 2H), 2.39 (t, 2H), 2.49-2.31 (m, 2H), 1.43 (d, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{21}\text{ClF}_3\text{N}_5\text{O}_2\text{S}$: 536. Observed 233 ($\text{M}^+ - 303$).

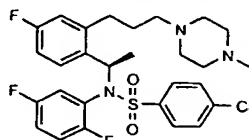
EXAMPLE 435

15 $R_f = 0.42$ (19:1 DCM:methanol). ^1H NMR (CDCl_3) δ (ppm): 7.62 (m, 2H), 7.47-7.37 (m, 2H), 7.00-6.50 (m, 6H), 5.90 (q, 1H), 3.08-2.98 (m, 1H), 2.70-2.60 (m, 1H), 2.53-2.38 (m, 6H), 1.92-1.82 (m, 2H), 1.70-1.63 (m, 4H), 1.51 (d, 3H), 1.50-1.44 (m, 2H). LC-MS calculated for $\text{C}_{28}\text{H}_{30}\text{ClF}_3\text{N}_2\text{O}_2\text{S}$: 551. Observed 551 (M^+).

20

EXAMPLE 436

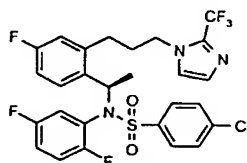
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(4-methyl-1-piperazinyl)propyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.4$ (9:1 DCM:methanol). ^1H NMR (CDCl_3) δ (ppm): 7.76-7.51 (m, 2H), 7.42-7.37 (m, 2H), 7.02-6.55 (m, 6H), 5.87 (q, 1H), 3.10-3.00 (m, 1H), 2.67-2.28 (m, 12H), 1.87-1.75 (m, 2H), 1.58-1.45 (m, 3H). LC-MS calculated for $\text{C}_{28}\text{H}_{31}\text{ClF}_2\text{N}_3\text{O}_2\text{S}$: 566. Observed 566 (M^+).

EXAMPLE 437

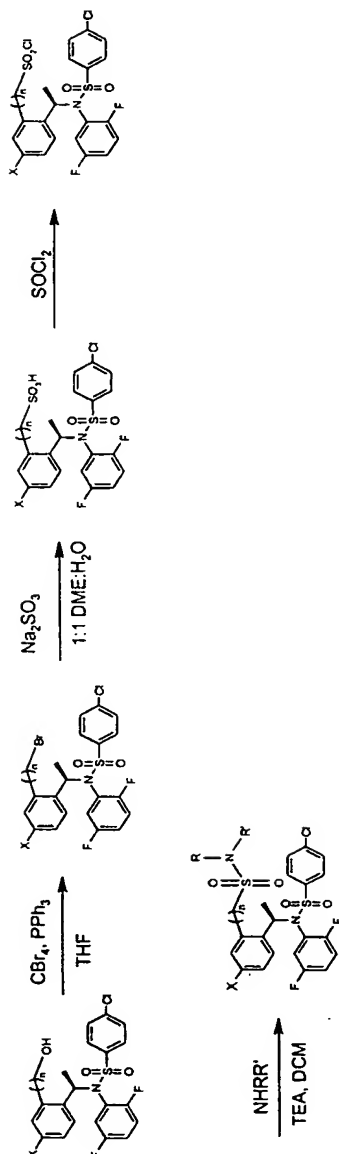
4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{3-[2-(trifluoromethyl)-1H-imidazol-1-yl]propyl}phenyl)ethyl]benzenesulfonamide



$R_f = 0.32$ (5:2; hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.74-7.40 (m, 6H), 7.01-6.23 (m, 6H), 5.87 (q, 1H), 4.19 (t, 2H), 3.01-2.96 (m, 2H), 2.32-2.16 (m, 2H), 1.44 (d, 3H). LC-MS calculated for $\text{C}_{27}\text{H}_{22}\text{ClF}_6\text{N}_3\text{O}_2\text{S}$: 602. Observed: 602 (M^+).

EXAMPLE 438

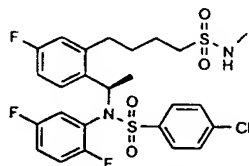
Numerous compounds according to the invention can be prepared employing the general scheme set forth in SCHEME 438.

SCHEME 438

Using the preparative scheme outlined in Example 438, the compounds of Examples 439-448 were prepared.

EXAMPLE 439

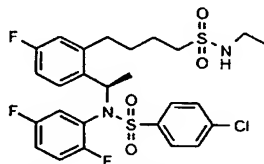
4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-
[(methylamino)sulfonyl]butyl}phenyl)ethyl]benzenesulfonamide



$R_f = 0.19$ (2:1; hexanes:ethyl acetate). ^1H NMR (300MHz CDCl_3) δ : 7.70-7.45 (m, 4H), 7.01-6.32 (m, 6H), 5.89 (q, 1H), 4.95 (m, 2H), 3.22-3.07 (m, 3H), 2.81-2.80 (m overlaps d, 4H), 2.03-1.84 (m, 4H), 1.49 (br, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{26}\text{ClF}_3\text{N}_2\text{O}_4\text{S}_2$ $[\text{M}^+]$ 575 Observed 272 ($\text{M}^+ - 303$).

EXAMPLE 440

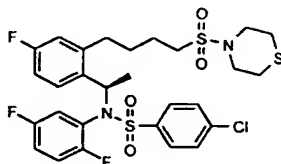
4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{4-[(ethylamino)sulfonyl]butyl}-4-fluorophenyl)ethyl]benzenesulfonamide



$R_f = 0.23$ (3:1; hexanes:ethyl acetate). ^1H NMR (300MHz CDCl_3) δ : 7.70-7.42 9m, 4H), 7.01-6.29 (m, 6H), 5.88 (q, 1H), 4.61 (t, 1H), 3.31-3.07 (m, 5H), 2.86-2.72(m, 1H), 2.03-1.78 (m, 4H), 1.48 (br, 3H), 1.21(t, 3H). LC-MS calculated for $\text{C}_{26}\text{H}_{28}\text{ClF}_3\text{N}_2\text{O}_4\text{S}_2$ $[\text{M}^+]$ 589; Observed: 286 ($\text{M}^+ - 303$).

EXAMPLE 441

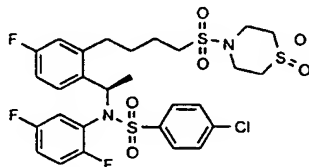
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(4-thiomorpholinylsulfonyl)butyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.41$ (3:1; hexanes:ethyl acetate). ^1H NMR (300MHz CDCl_3) δ : 7.70-7.40(m, 4H), 7.01-6.28(m, 6H), 5.88 (q, 1H), 3.65-3.60 (m, 4H), 3.17-3.05 (m, 3H), 2.83-2.69 (m, 5H), 2.10-1.81 (m, 4H), 1.50 (br d, 3H). LC-MS calculated for $\text{C}_{28}\text{H}_{30}\text{ClF}_3\text{N}_2\text{O}_4\text{S}_3$ $[\text{M}^+]$ 647.2; Observed: 647.

EXAMPLE 442

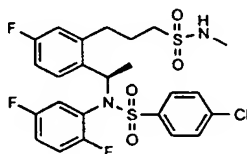
4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{4-[(1,1-dioxido-4-thiomorpholinyl)sulfonyl]butyl}-4-fluorophenyl)ethyl]benzenesulfonamide



5 $R_f = 0.32$ (2:1; hexanes:ethyl acetate). $^1\text{H NMR}$ (300MHz CDCl_3) δ : 7.70-7.38 (m, 4H), 6.90-6.31 (m, 6H), 6.00 (m, 1H), 4.10-3.98 (m, 4H), 3.41-2.92 (m, 8H), 2.22-1.93 (m, 4H), 1.58 (d, 3H). LC-MS calculated for $\text{C}_{28}\text{H}_{30}\text{ClF}_3\text{N}_2\text{O}_6\text{S}_3$ $[\text{M}^+]$ 679.2; Observed: 376 ($\text{M}^+ - 303$).

EXAMPLE 443

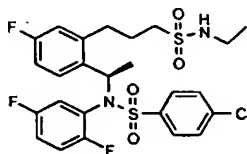
4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{3-[(methylamino)sulfonyl]propyl}phenyl)ethyl]benzenesulfonamide



10 $R_f = 0.18$ (3:1 hexanes:ethyl acetate) $^1\text{H NMR}$ (300MHz CDCl_3) δ : 7.71-7.47 (m, 4H), 7.01-6.30 (m, 6H), 5.94-5.91 (br, 1H), 4.73 (br, 1H), 3.24-3.22 (m, 3H), 3.05-2.83 (m, 4H), 2.20 (br, 2H), 1.45 (s, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{24}\text{ClF}_3\text{N}_2\text{O}_4\text{S}_2$ $[\text{M}^+]$ 561; Observed: 258 ($\text{M}^+ - 303$).

EXAMPLE 444

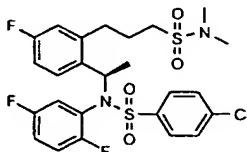
4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{3-[(ethylamino)sulfonyl]propyl}-4-fluorophenyl)ethyl]benzenesulfonamide



15 $R_f = 0.30$ (3:1 hexanes:ethyl acetate) $^1\text{H NMR}$ (300MHz CDCl_3) δ : 7.72-7.60 (m, 2H), 7.49-7.42 (m, 2H), 7.05-6.30 (m, 6H), 5.95-5.88 (q, 1H), 4.79-4.75 (t, 1H), 3.25-3.17 (m, 5H), 3.00-2.92 (m, 1H), 2.24-2.14 (m, 2H), 1.48-1.46 (m, 3H), 1.25-1.18 (m, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{26}\text{ClF}_3\text{N}_2\text{O}_4\text{S}_2$ $[\text{M}^+]$ 575; Observed: 272 ($\text{M}^+ - 303$).

EXAMPLE 445

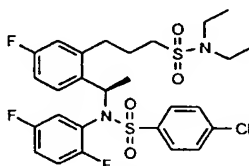
4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{3-[(dimethylamino)sulfonyl]propyl}-4-fluorophenyl)ethyl]benzenesulfonamide



5 $R_f = 0.26$ (3:1 hexanes:ethyl acetate) $^1\text{H NMR}$ (300MHz CDCl_3) δ (ppm): 7.68-7.47 (m, 4H), 7.08-6.30 (m, 6H), 5.89 (br, 1H), 3.14-2.88 (m, 10H), 2.22 (m, 2H) 1.48-1.46 (br, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{26}\text{ClF}_3\text{N}_2\text{O}_4\text{S}_2$ $[\text{M}^+]$ 575; Observed: 575.

EXAMPLE 446

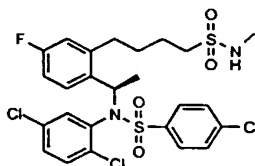
4-chloro-N-[(1R)-1-(2-{3-[(diethylamino)sulfonyl]propyl}-4-fluorophenyl)ethyl]-N-(2,5-difluorophenyl)benzenesulfonamide



10 $R_f = 0.35$ (3:1 hexanes:ethyl acetate) $^1\text{H NMR}$ (300MHz CDCl_3) δ (ppm): 7.69-7.44 (m, 4H), 7.03-6.31 (m, 6H), 5.88-5.86 (q, 1H), 3.37-3.09 (m, 8H), 2.20-2.15 (m, 2H), 1.49-1.47 (m, 3H), 1.25-1.19 (m, 6H). LC-MS calculated for $\text{C}_{27}\text{H}_{30}\text{ClF}_3\text{N}_2\text{O}_4\text{S}_2$ $[\text{M}^+]$ 603; Observed: 603.

EXAMPLE 447

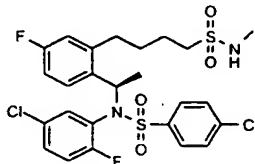
4-chloro-N-(2,5-dichlorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[(methylamino)sulfonyl]butyl}phenyl)ethyl]benzenesulfonamide



15
20 $R_f = 0.27$ (2:1 hexanes:ethyl acetate) $^1\text{H NMR}$ (300MHz CDCl_3) δ (ppm): 7.71 (d, 2H), 7.50-7.47 (d, 2H), 7.36-7.15 (m, 2H), 6.91-6.72 (m, 2H), 6.56-6.37 (m, 2H), 5.92-5.77 (m, 1H), 4.60-4.48 (m, 1H), 3.24-3.12 (m, 3H), 2.84-2.69 (m, 4H), 2.06-1.74 (m, 4H), 1.44-1.37 (m, 3H). LC-MS caclcd for $\text{C}_{25}\text{H}_{26}\text{Cl}_3\text{FN}_2\text{O}_4\text{S}_2$ $[\text{MH}^+]$ 608; Observed: 608.

EXAMPLE 448

4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[(methylamino)sulfonyl]butyl}phenyl)ethyl]benzenesulfonamide

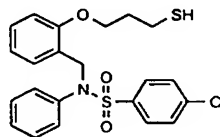


5 $R_f = 0.22$ (2:1 hexanes:ethyl acetate) $^1\text{H NMR}$ (300MHz CDCl_3) δ (ppm): 7.68-7.58 (m, 2H), 7.49-7.41 (m, 2H), 7.25-6.51 (m, 6H), 5.91-5.89 (m, 1H), 4.50-4.48 (br, 1H), 3.21-3.01 (m, 3H), 2.84-2.82 (m, 4H), 2.01-1.83 (m, 4H), 1.49-1.47 (br, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{26}\text{Cl}_2\text{F}_2\text{N}_2\text{O}_4\text{S}_2$ $[\text{M}^+]$ 591; Observed: 288 ($\text{M}^+ - 303$).

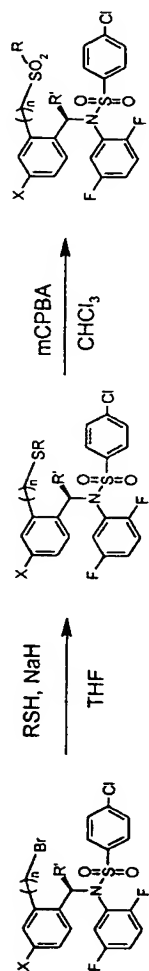
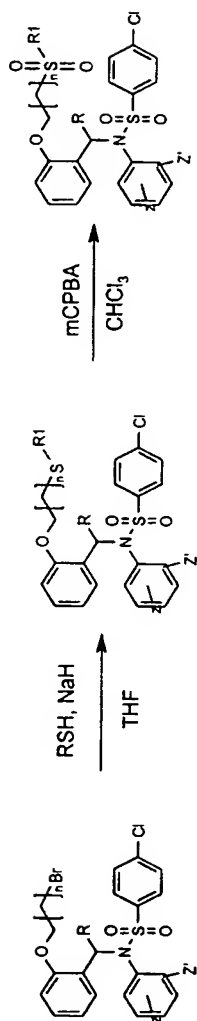
10

EXAMPLE 449

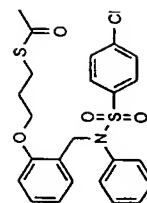
4-chloro-N-phenyl-N-[2-(3-sulfanylpropoxy)benzyl]benzenesulfonamide



15 Numerous compounds according to the invention can be prepared employing the general scheme set forth in SCHEME 449.

SCHEME 449

$\text{R}' = \text{H}, \text{CH}_3$
 $n = 1-4$
 $x = \text{H}, \text{F}$



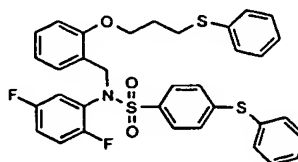
To a stirred solution of N-2-(3-bromopropoxy)benzyl 4-chlorobenzenesulfanilide (200 mg, 0.4 mmol) in DMF (5 mL) was added the potassium salt of thioacetic acid (92 mg, 0.81 mmol). The reaction mixture was then warmed to 60 °C. After 3 h, the reaction mixture was cooled to room temperature, diluted with ethyl acetate (25 mL), washed with saturated bicarbonate solution (3x 10 mL) and saturated brine (2x 10 mL), dried with MgSO₄, filtered and concentrated under reduced pressure to isolate a colorless oil which was purified by SiO₂ chromatography (7:1, hexanes:ethyl acetate) to afford the desired product (130 mg, y: 63%). $R_f = 0.25$ (20% ethyl acetate/hexanes) ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.60-7.56 (m, 2H), 7.46-7.42 (m, 2H), 7.36 (dd, 1H), 7.23-7.7.12 (dd, 2H), 6.85 (t, 1H), 6.70 (d, 1H), 4.82 (s, 2H), 3.85 (t, 2H), 2.95 (t, 2H), 2.33 (s, 3H), 1.92 (q, 2H), ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 196.0, 156.7, 139.6, 139.4, 137.5, 130.7, 129.5, 129.3, 129.3, 128.3, 124.5, 121.0, 111.3, 66.4, 49.8, 31.1, 29.6, 26.2.

A stirred solution of thioacetate analog prepared above (100 mg, 0.2 mmol) at °C in ethanol (5 mL) was vigorously degassed for 0.5 h, then a solution of degassed 1.0 N NaOH (0.4 mL, 0.4 mmol) was added. The reaction mixture was allowed stir at 0 °C for 1h, warmed to room temperature and stirred at room temperature for 1h, then diluted with degassed ethyl acetate (20 mL), washed with saturated bicarbonate solution (3x 10 mL), 10% aqueous HCl (3x 10 mL), dried with MgSO₄, filtered and concentrated under reduced pressure to isolate a white solid. The crude material was purified by chromatography on SiO₂ (4:1 hexanes:ethyl acetate) to give 40 mg of product (y: 44%). $R_f = 0.25$ (20% ethyl acetate/hexanes) ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.58-7.56 (m, 2H), 7.47-7.54 (m, 2H), 7.34-7.14 (m, 5H), 6.99 (m, 2H), 6.87-6.73 (dt, 2H), 4.78 (s, 2H), 3.92 (t, 2H), 2.63 (q, 2H), 1.96 (q, 2H), 1.35 (t, 1H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 159.1, 141.9, 141.8, 139.9, 133.1, 131.8, 131.8, 131.7, 131.6, 130.6, 126.7, 123.2, 113.7, 68.2, 52.2, 35.8, 24.0.

Using the preparative scheme outlined above, the compounds of Examples 450-464 were prepared.

EXAMPLE 450

N-(2,5-difluorophenyl)-4-(phenylsulfanyl)-N-{2-[3-(phenylsulfanyl)propoxy]benzyl}benzenesulfonamide



WO 00/50391

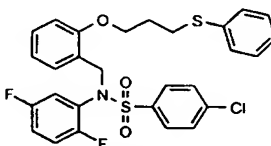
230

PCT/US00/04560

$R_f = 0.54$ (4:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.63 (d, 2H), 7.54-7.50 (m, 5H), 7.33-7.26 (m, 6H), 7.18 (t, 5H), 6.97 (m, 1H), 6.87-6.79 (m, 2H), 4.70 (s, 2H), 3.94 (t, 2H), 3.08 (t, 2H), 1.90-1.86 (m, 2H).

EXAMPLE 451

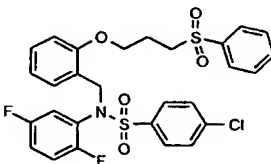
4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(phenylsulfanyl)propoxy]benzyl}benzenesulfonamide



$R_f = 0.45$ (6:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, DMSO) δ (ppm): 7.72 (q, 4H), 7.34-7.18 (m, 8H), 7.00-6.98 (m, 2H), 6.89-6.80 (m, 2H), 4.73 (s, 2H), 3.95 (t, 2H), 3.09 (t, 2H), 1.91-1.87 (m, 2H).

EXAMPLE 452

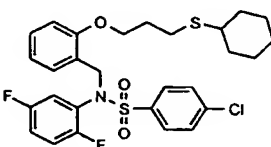
4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(phenylsulfonyl)propoxy]benzyl}benzenesulfonamide



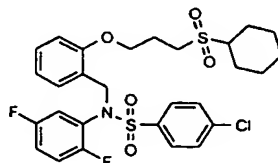
$R_f = 0.40$ (3:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.96 (d, 2H), 7.68-7.54 (m, 5H), 7.47 (d, 2H), 7.19-7.10 (m, 2H), 6.93-6.68 (m, 5H), 4.77 (s, 2H), 3.97 (t, 2H), 3.38 (t, 2H), 2.24-2.15 (m, 2H).

EXAMPLE 453

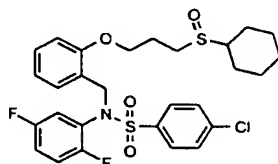
4-chloro-N-{2-[3-(cyclohexylsulfanyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide



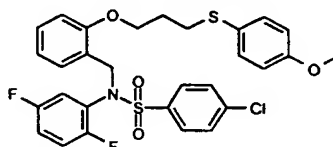
$R_f = 0.26$ (5% methanol in DCM), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.66 (d, 2H), 7.47 (m, 2H), 7.28-7.15 (m, 1H), 7.00 (d, 1H), 6.90 (m, 2H), 6.75 (m, 3H), 4.81 (s, 2H), 3.92 (m, 2H), 2.66 (m, 3H), 1.94 (m, 4H), 1.75 (m, 2H), 1.60 (m, 2H), 1.28 (m, 4H).

EXAMPLE 454**4-chloro-N-{2-[3-(cyclohexylsulfonyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide**

$R_f = 0.29$ (3:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.65 (d, 2H), 7.48 (d, 2H), 7.18 (t, 1H), 7.80 (d, 2H), 6.90 (m, 2H), 6.76 (m, 3H), 4.78 (s, 2H), 4.10 (t, 2H), 3.29 (t, 2H), 2.94 (m, 1H), 2.35 (m, 2H), 2.22 (d, 2H), 1.90 (m, 2H), 1.72-1.19 (m, 6H). MS calculated for $\text{C}_{28}\text{H}_{30}\text{ClF}_2\text{NO}_5\text{S}_2$, $[\text{MNa}^+]$ 620; Observed: 620.

EXAMPLE 455**4-chloro-N-{2-[3-(cyclohexylsulfinyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide**

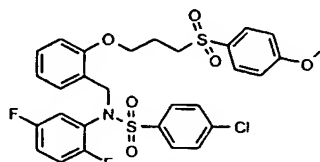
$R_f = 0.32$ (1:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.64 (d, 2H), 7.47 (d, 2H), 7.19 (t, 1H), 7.08 (d, 2H), 6.92-6.87 (m, 2H), 6.80-6.76 (m, 3H), 4.79 (s, 2H), 4.16-3.98 (m, 2H), 3.12-3.03 (m, 1H), 2.87-2.78 (m, 1H), 2.67-2.60 (m, 1H), 2.34 (m, 2H), 2.14 (d, 1H), 1.95-1.69 (m, 3H), 1.57-1.24 (m, 6H). MS calculated for $\text{C}_{28}\text{H}_{30}\text{ClF}_2\text{NO}_4\text{S}_2$, $[\text{MH}]$ 582; Observed: 582.

EXAMPLE 456**N-(4-bromophenyl)-4-chloro-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride**

$R_f = 0.44$ (6:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.67-7.64 (m, 2H), 7.48-7.44 (m, 2H), 7.35-7.32 (m, 2H), 7.31-7.15 (m, 3H), 6.91-6.70 (m, 8H), 4.77 (m, 2H), 3.94-3.86 (m, 2H), 3.77 (m, 3H), 2.97-2.92 (m, 2H), 1.97-1.88 (m, 2H). MS calculated for $\text{C}_{29}\text{H}_{26}\text{ClF}_2\text{NO}_4\text{S}_2$, $[\text{MNa}^+]$ 612; Observed: 612.

EXAMPLE 457

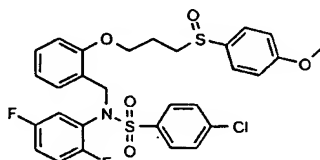
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-methoxyphenyl)sulfonyl]propoxy}benzyl)benzenesulfonamide



$R_f = 0.42$ (2:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.87 (d, 2H), 7.63 (d, 2H), 7.47 (d, 2H), 7.26-7.11 (m, 2H), 7.00 (d, 2H), 6.91-6.75 (m, 4H), 6.69 (d, 1H), 4.74 (s, 2H), 3.96 (t, 2H), 3.86 (s, 3H), 3.36-3.31 (m, 2H), 2.22-2.13 (m, 2H). MS calculated for $\text{C}_{29}\text{H}_{26}\text{ClF}_2\text{NO}_6\text{S}_2$, $[\text{MNa}^+]$ 644; Observed: 644.

EXAMPLE 458

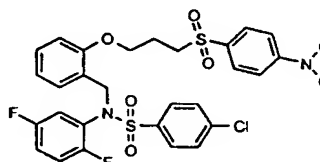
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-methoxyphenyl)sulfinyl]propoxy}benzyl)benzenesulfonamide



$R_f = 0.23$ (1:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.66-7.54 (m, 4H), 7.49 (d, 2H), 7.20-7.11 (m, 2H), 7.03 (d, 2H), 6.94-6.76 (m, 4H), 6.71 (d, 1H), 4.76 (s, 2H), 4.05-3.84 (m, 5H), 3.15-2.90 (m, 2H), 2.26-2.00 (m, 2H). MS calculated for $\text{C}_{29}\text{H}_{26}\text{ClF}_2\text{NO}_5\text{S}_2$, $[\text{MNa}^+]$ 628; Observed: 628.

EXAMPLE 459

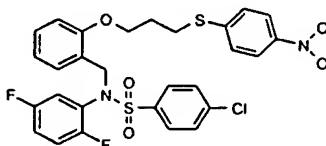
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-nitrophenyl)sulfonyl]propoxy}benzyl)benzenesulfonamide



$R_f = 0.56$ (2:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 8.40 (d, 2H), 8.25 (d, 2H), 7.59 (d, 2H), 7.48 (d, 2H), 7.19-7.14 (t, 1H), 6.89-6.82 (m, 3H), 6.75-6.64 (m, 3H), 4.73 (s, 2H), 4.1 (t, 2H), 3.65 (m, 2H), 2.38-2.33 (m, 2H).

EXAMPLE 460

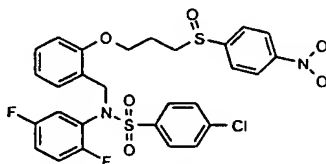
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-nitrophenyl)sulfanyl]propoxy}benzyl)benzenesulfonamide



$R_f = 0.40$ (6:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 8.12-8.09 (m, 2H), 7.67-7.63 (m, 2H), 7.49-7.45 (m, 2H), 7.41-7.37 (m, 2H), 7.22-7.16 (m, 1H), 7.12-7.09 (m, 1H), 6.91-6.74 (m, 5H), 4.82 (s, 2H), 4.05 (t, 2H), 3.32 (t, 2H), 2.19 (m, 2H).

EXAMPLE 461

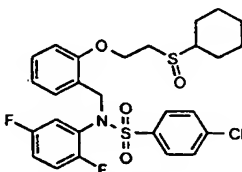
4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-nitrophenyl)sulfinyl]propoxy}benzyl)benzenesulfonamide



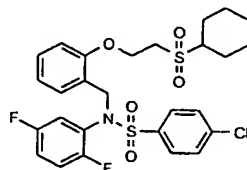
$R_f = 0.53$ (1:1 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 8.36 (d, 2H), 7.93 (d, 2H), 7.64 (d, 2H), 7.50 (d, 2H), 7.17 (m, 1H), 6.91-6.80 (m, 3H), 6.74-6.65 (m, 3H), 4.76 (s, 2H), 4.19-4.02 (m, 2H), 3.56-3.47 (m, 1H), 3.23-3.14 (m, 1H), 2.47-2.41 (m, 1H), 2.17-2.13 (m, 1H).

EXAMPLE 462

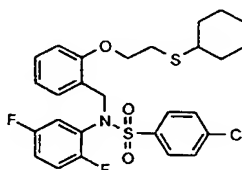
4-chloro-N-{2-[2-(cyclohexylsulfinyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide



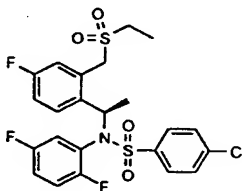
$R_f = 0.35$ (1:2 hexanes:ethyl acetate), ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.65 (d, 2H), 7.47 (d, 2H), 7.22-7.11 (m, 2H), 6.94-6.80 (m, 5H), 4.84 (d, 1H), 4.70 (d, 1H), 4.47-4.27 (m, 2H), 3.19-3.10 (m, 1H), 2.94 (dt, 1H), 2.65 (tt, 1H), 2.14 (d, 1H), 2.04-1.88 (m, 3H), 1.73 (m, 1H), 1.59-1.25 (m, 4H).

EXAMPLE 463**4-chloro-N-{2-[2-(cyclohexylsulfonyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide**

$R_f = 0.30$ (3:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.65 (d, 2H), 7.47 (d, 2H), 7.26-7.18 (m, 2H), 6.97-6.81 (m, 5H), 4.78 (s, 2H), 4.35 (t, 2H), 3.38 (t, 2H), 2.92 (tr, 1H), 2.20 (d, 2H), 2.05 (m, 2H), 1.74-1.55 (m, 3H), 1.334-1.20 (m, 3H).

EXAMPLE 464**4-chloro-N-{2-[2-(cyclohexylsulfanyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide**

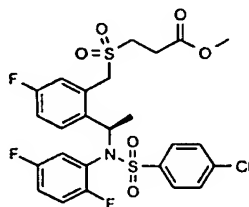
$R_f = 0.30$ (15:1 hexanes:ethyl acetate), $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.67 (d, 2H), 7.56 (d, 2H), 7.34 (d, 1H), 7.19 (t, 1H), 6.95-6.86 (m, 4H), 6.72 (d, 1H), 4.79 (s, 2H), 3.93 (t, 2H), 2.74 (t, 2H), 2.67 (m, 1H), 1.95 (br, 2H), 1.77 (br, 2H), 1.63-1.27 (m, 6H).

EXAMPLE 465**4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[(ethylsulfonyl)methyl]-4-fluorophenyl}ethyl)benzenesulfonamide**

$R_f = 0.4$ (3:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.75-7.65 (m, 2H), 7.55-7.44 (m, 2H), 7.17-6.24 (m, 6H), 6.08 (q, 1H), 5.56 (overlapping doublets, 1H), 4.17 (overlapping doublets, 1H), 3.30-3.20 (m, 2H), 1.61-1.55 (m, 3H), 1.34 (d, 3H). LC-MS calculated for $\text{C}_{23}\text{H}_{21}\text{ClF}_3\text{NO}_4\text{S}_2$ $[\text{M}^+]$ 532; Observed: 229 ($\text{M}^+ - 303$).

EXAMPLE 466

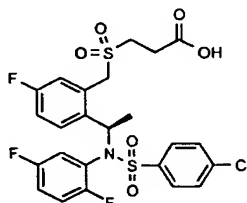
methyl 3-{[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl]sulfonyl}propanoate



$R_f = 0.50$ (2:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.81-7.67 (m, 2H), 7.57-7.47 (m, 2H), 7.17-6.27 (m, 6H), 6.15-6.03 (m, 1H), 5.62-5.58 (overlapping doublets, 1H), 4.26-4.22 (overlapping doublets, 1H), 3.80 (s, 3H), 3.72-3.51 (m, 2H), 3.12-3.05 (m, 2H), 1.39-1.25 (br, 3H). LC-MS calcd for $\text{C}_{25}\text{H}_{23}\text{ClF}_3\text{NO}_6\text{S}_2$: 590. Observed : 608 ($\text{M}^+ + \text{H}_2\text{O}$).

EXAMPLE 467

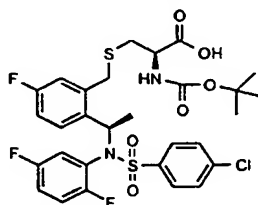
3-{[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl]sulfonyl}propanoic acid



$R_f = 0.55$ (6:1;DCM:methanol). $^1\text{H NMR}$ (CD_3OD) δ (ppm): 7.83-7.54 (m, 4H), 7.21- 6.32 (m, 6H), 6.10-6.07 (m, 1H), 5.49-5.44 (m, 1H), 4.64-4.53 (m, 1H), 3.64-3.51 (m, 2H), 3.05-2.93 (m, 2H), 1.38 (d, 3H). LC-MS calcd for $\text{C}_{24}\text{H}_{21}\text{ClF}_3\text{NO}_6\text{S}_2$: 576. Observed : 576 (M^+).

EXAMPLE 468

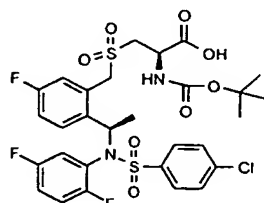
methyl (2R)-2-[(tert-butoxycarbonyl)amino]-3-{[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl]sulfonyl}propanoate



$R_f = 0.47$ (3:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.74-7.63(m, 2H), 7.49-7.39 (m, 2H), 7.05-6.41(m, 6H), 6.05 (br, 1H), 5.53 (br, 1H), 4.68-4.62 (m, 1H), 4.47-4.38 (m, 1H), 3.81-3.76 9m, 4H0, 3.07-2.97 (m, 2H), 1.48-1.37 (br overlaps s, 12H). LC-MS calcd for $\text{C}_{30}\text{H}_{32}\text{ClF}_3\text{N}_2\text{O}_6\text{S}_2$: 673. Observed : 573 ($\text{M}^+ - \text{Boc}$).

EXAMPLE 469

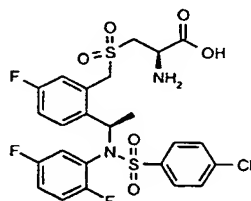
methyl (2R)-2-[(tert-butoxycarbonyl)amino]-3-[[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorobenzyl]sulfonyl]propanoate



$R_f = 0.25$ (3:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.80—7.69 (m, 2H), 7.58-7.47 (m, 2H), 7.16-7.01 (m, 2H), 6.89-6.62 (m, 3H), 6.31-5.91 (m, 2H), 5.61 (br, 1H), 4.91 (br, 1H), 4.31-4.21 (m, 1H), 3.92-3.84 (m overlaps s, 5H), 1.50 (s, 9H), 1.36-1.34 (br, 3H). LC-MS calcd for $\text{C}_{30}\text{H}_{32}\text{ClF}_3\text{N}_2\text{O}_8\text{S}_2$: 705. Observed : 605 ($\text{M}^+ - \text{Boc}$).

EXAMPLE 470

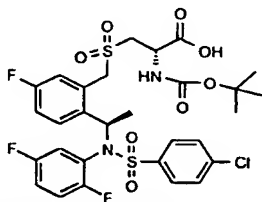
methyl 2-amino-3-[[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorobenzyl]sulfonyl]propanoate hydrochloride



$R_f = 0.50$ (2:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.76-7.64 (m, 2H), 7.53-7.43 (m, 2H), 7.24-7.16 (m, 1H), 7.05-6.33 (m, 5H), 6.13 (br, 1H), 5.57 9d, 1H), 4.82-4.68 (m, 2H), 3.84-3.0 (br overlaps s, 7H), 137-1.35 (br, 3H).. LC-MS calcd for $\text{C}_{25}\text{H}_{24}\text{ClF}_3\text{N}_2\text{O}_6\text{S}_2$: 604. Observed : 605 (MH^+).

EXAMPLE 471

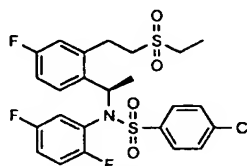
methyl (2S)-2-[(tert-butoxycarbonyl)amino]-3-[[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorobenzyl]sulfonyl]propanoate



$R_f = 0.25$ (2:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.76-7.63 (m, 2H), 7.53-7.41 (m, 2H), 7.71-7.00 (m, 3H), 6.87-6.32 (m, 3H), 6.11-5.81 (m, 2H), 5.63 (m, 1H), 4.81 (br, 1H), 4.59-4.23 (m, 1H), 3.94-3.88 (m, 2H), 3.85 (s, 3H), 1.48 (s, 9H), 1.37-1.35 (br, 3H). LC-MS calcd for $\text{C}_{30}\text{H}_{32}\text{ClF}_3\text{N}_2\text{O}_8\text{S}_2$: 705. Observed : 605 ($\text{M}^+ - \text{Boc}$).

EXAMPLE 472

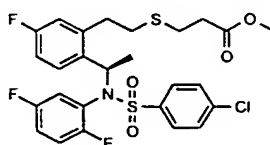
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(ethylsulfonyl)ethyl]-4-fluorophenyl}ethyl)benzenesulfonamide



$R_f = 0.28$ (3:1; hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.68-7.58 (m, 2H), 7.49-7.48 (m, 2H), 7.05-6.41 (m, 6H), 5.89 (q, 1H), 3.54-3.20 (m, 6H), 1.50-1.41 (m, 6H). LC-MS calculated for $\text{C}_{24}\text{H}_{23}\text{ClF}_3\text{NO}_4\text{S}_2$ 546; Observed: 242 ($\text{M}^+ - 303$).

EXAMPLE 473

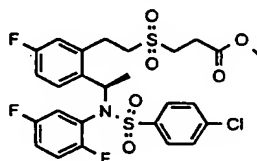
methyl 3-({2-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl}ethyl)sulfanyl)propanoate



$R_f = 0.33$ (6:1; hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.67-7.54 (m, 2H), 7.44-7.35 (m, 2H), 7.00-6.28 (m, 6H), 5.93-5.81 (m, 1H), 3.68 (s, 3H), 3.40-3.28 (m, 1H), 2.99-2.65 (m, 7H), 1.53 (br 3H). LC-MS calcd for $\text{C}_{26}\text{H}_{25}\text{ClF}_3\text{NO}_4\text{S}_2$: 572. Observed: 269 ($\text{M}^+ - 303$).

EXAMPLE 474

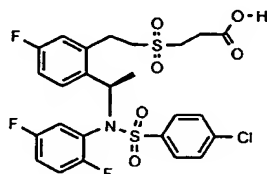
methyl 3-({2-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl}ethyl)sulfonyl)propanoate



$R_f = 0.50$ (2:1; hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.72-7.59 (m, 2H), 7.50-7.40 (m, 2H), 7.08-6.42 (m, 6H), 5.97-5.83 (m, 1H), 3.72 (s, 3H), 3.57-3.34 (m, 6H), 2.98 (t, 3H), 1.50-1.38 (br 3H). LC-MS calcd for $\text{C}_{26}\text{H}_{25}\text{ClF}_3\text{NO}_6\text{S}_2$: 640. Observed: 621 ($\text{M}^+ + \text{H}_2\text{O}$).

EXAMPLE 475

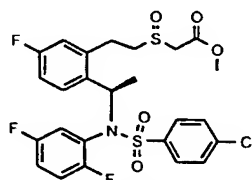
3-({2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}-5-fluorophenyl]ethyl}sulfonyl)propanoic acid



$R_f = 0.48$ (10:1;DCM:methanol). ^1H NMR (CD_3OD) δ (ppm): 7.89-7.63 (m, 2H), 7.58-7.51(m, 2H), 7.21-7.00 (m, 3H), 6.89-6.45 (m, 3H), 5.95-5.90(m, 1H), 3.60-3.50 (m, 4H), 3.23-3.22 (m, 2H), 2.91-2.83 (m, 2H), 1.55-1.42 (br, 3H). LC-MS calcd for $\text{C}_{25}\text{H}_{23}\text{ClF}_3\text{NO}_6\text{S}_2$: 589. Observed : 589 (M^+).

EXAMPLE 476

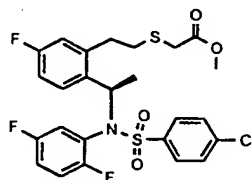
methyl ({2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}-5-fluorophenyl]ethyl}sulfonyl)acetate



$R_f = 0.45$ (1:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.75-7.58 (m,2H), 7.50-7.40 (m, 2H), 7.08-6.88 (m, 3H), 6.88-6.42 (m, 3H), 5.92-5.87 (m,1H), 3.98-3.79 (m overlaps s, 5H), 3.59-3.21 (m, 4H), 1.49-1.44 (m, 3H). LC-MS calcd for $\text{C}_{25}\text{H}_{23}\text{ClF}_3\text{NO}_5\text{S}_2$: 574. Observed : 271 ($\text{M}^+ - 303$).

EXAMPLE 477

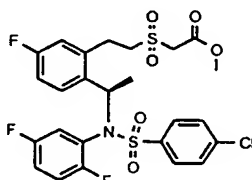
methyl ({2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}-5-fluorophenyl]ethyl}sulfonyl)acetate



$R_f = 0.40$ (6:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.71-7.58 (m, 2H), 7.48-7.39 (m, 2H), 7.01-6.33 (m, 6H), 5.90 (q, 1H), 3.78 (s, 3H), 3.47-3.45 (m, 3H), 3.00-2.91 (m, 3H), 1.55-1.47 (br, 3H). LC-MS calcd for $\text{C}_{25}\text{H}_{23}\text{ClF}_3\text{NO}_4\text{S}_2$: 558. Observed : 255 ($\text{M}^+ - 303$).

EXAMPLE 478

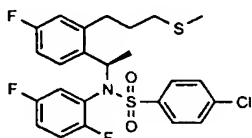
methyl ({2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl)sulfonyl)acetate



$R_f = 0.45$ (2:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.71-7.61 (m, 2H), 7.51-7.39 (m, 2H), 7.07-6.37 (m, 6H), 5.95-5.89(m, 1H), 4.39-4.34 (m, 1H), 4.15-4.10 (m, 1H), 3.87 (s, 3H), 3.75-3.61 (m, 3H), 3.41-3.31 (m, 1H), 1.51-1.41 (br, 3H). LC-MS calcd for $\text{C}_{25}\text{H}_{23}\text{ClF}_3\text{NO}_6\text{S}_2$: 590. Observed : 287 ($\text{M}^+ - 303$).

EXAMPLE 479

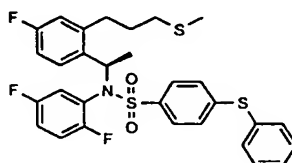
methyl ({2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl)sulfonyl)acetate



$R_f = 0.30$ (10:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.71-7.57 (m, 2H), 7.44-7.37 (m, 2H), 7.00-6.31 (m, 6H), 5.88 (q, 1H), 3.21-3.09 (m, 1H), 2.83-2.73 (m, 1H), 2.62 (m, 2H), 2.16 (s, 3H), 1.99-1.89 (m, 2H), 1.54 (br, 3H).). LC-MS calculated for $\text{C}_{24}\text{H}_{23}\text{ClF}_3\text{NO}_2\text{S}_2$ [M^+] 514; Observed: 211 ($\text{M}^+ - 303$).

EXAMPLE 480

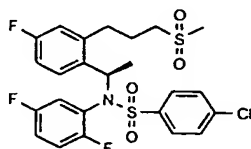
N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(methylsulfanyl)propyl]phenyl}ethyl)-4-(methylsulfanyl)benzenesulfonamide



$R_f = 0.39$ (5:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.64-7.50-(m, 2H), 7.23-7.15 (m, 2H), 7.00-6.84 (m, 3H), 6.69-6.33 (m, 3H), 5.88-5.79 (m, 1H), 2.21-3.10(m, 1H), 2.78-2.72 (m, 1H), 2.61 9t, 2H), 2.49 9s, 3H), 2.14 (s, 3H), 1.98-1.90 (m, 2H), 1.54-1.50 (br, 3H).). LC-MS calculated for $\text{C}_{25}\text{H}_{26}\text{F}_3\text{NO}_2\text{S}_3$ [M^+] 525; Observed: 548 ($\text{M} + \text{Na}$).

EXAMPLE 481

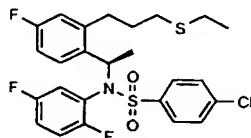
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(methylsulfonyl)propyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.19$ (2:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.73-7.59 (m, 2H), 7.51-7.41 (m, 2H), 7.05-6.30-(m, 6H), 5.91 (q, 1H), 3.24-3.03 (m, 4H), 2.98 (s, 3H), 2.27-2.23 (m, 2H), 1.45 (d, 3H). LC-MS calculated for $\text{C}_{24}\text{H}_{23}\text{ClF}_3\text{NO}_4\text{S}_2$ $[\text{M}^+]$ 546; Observed: 243 ($\text{M}^+ - 303$).

EXAMPLE 482

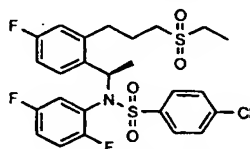
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(ethylsulfonyl)propyl]-4-fluorophenyl}ethyl)benzenesulfonamide



$R_f = 0.31$ (10:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.68-7.54 (m, 2H), 7.44-7.38 (m, 2H), 7.00-6.28 (m, 6H), 5.87 (q, 1H), 3.22-3.08 (m, 1H), 2.82-2.53 (m, 5H), 1.98-1.86 (m, 2H), 1.55 (br, 3H), 1.30 (t, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{25}\text{ClF}_3\text{NO}_4\text{S}_2$ $[\text{M}^+]$ 528; Observed: 225 ($\text{M}^+ - 303$).

EXAMPLE 483

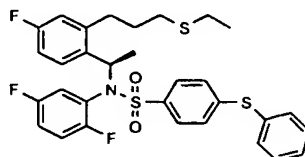
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(ethylsulfonyl)propyl]-4-fluorophenyl}ethyl)benzenesulfonamide



$R_f = 0.45$ (2:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.71-7.60 (m, 2H), 7.52-7.40 (m, 2H), 7.01-6.31(m, 6H), 5.90 (q, 1H), 3.22-2.87 (m, 6H), 2.33-2.19 (m, 2H), 1.45-1.40 (m, 6H). LC-MS calculated for $\text{C}_{25}\text{H}_{25}\text{ClF}_3\text{NO}_4\text{S}_2$ $[\text{M}^+]$ 560; Observed: 257 ($\text{M}^+ - 303$).

EXAMPLE 484

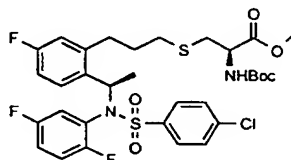
N-(2,5-difluorophenyl)-4-(ethylsulfanyl)-N-((1R)-1-{2-[3-(ethylsulfanyl)propyl]-4-fluorophenyl}ethyl)benzenesulfonamide



$R_f = 0.49$ (5:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm) : 7.68-7.50 (m, 2H), 7.29-7.21(m, 2H), 7.04-6.33 (m, 6H), 5.88-5.76 (m, 1H), 3.21-3.11 9m, 1H, 2.98 9q, 2H, 2.83-2.71 (m, 1H), 2.68-2.56 (m overlaps q, 4H), 1.95-1.93 9m, 2H), 1.52-1.49 (br, 3H), 1.33 (t, 3H), 1.27 (t, 3H). LC-MS calcd for $\text{C}_{27}\text{H}_{30}\text{F}_3\text{NO}_2\text{S}_3$: 553. Observed : 576 ($\text{M}^+ + \text{Na}$).

EXAMPLE 485

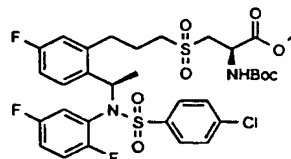
methyl (2R)-2-[(tert-butoxycarbonyl)amino]-3-({3-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl}propyl)sulfanyl)propanoate



$R_f = 0.50$ (3:1;hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.71-7.58 (m, 2H), 7.45-7.40 (m, 2H), 7.00-6.45 (m, 6H), 5.87 (q, 1H), 4.45-5.40 (br, 1H), 4.61 (br, 1H), 3.78, 3.76 (s, rotomers, 3H), 3.30-3.00 (m, 3H), 2.81-2.65 (m, 3H), 1.94-1.88 (m, 2H), 1.52-1.38 (br overlaps s, 12H). LC-MS calcd for $\text{C}_{32}\text{H}_{36}\text{ClF}_3\text{N}_2\text{O}_6\text{S}_2$: 701. Observed : 398 ($\text{M}^+ - 303$).

EXAMPLE 486

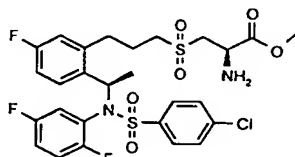
methyl (2R)-2-[(tert-butoxycarbonyl)amino]-3-({3-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl}propyl)sulfonyl)propanoate



$R_f = 0.38$ (2:1; hexanes:ethyl acetate). $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.71-7.61 (m,2H), 7.50-7.41 (m, 2H), 7.11-6.49 (m, 6H), 5.89 (q, 1H), 5.71 (br, 1H), 3.81, 3.79 (s, rotomers, 3H), 3.74-3.70 (m,2H), 3.24-3.20 9m, 3H), 2.91 (br, 1H), 2.28-2.17 (m, 2H), 1.45-1.45 (br overlaps s, 12H). LC-MS calcd for $\text{C}_{32}\text{H}_{36}\text{ClF}_3\text{N}_2\text{O}_8\text{S}_2$: 733. Observed : 633 ($\text{M}^+ - \text{Boc}$).

EXAMPLE 487

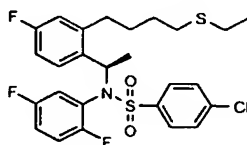
methyl (2R)-2-amino-3-({3-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl}propyl)sulfonyl)propanoate hydrochloride



$R_f = 0.43$ (2:1; hexanes:ethyl acetate). ^1H NMR (CD_3OD) δ (ppm): 7.81-7.51 (m, 4H), 7.70-6.85 (m, 4H), 6.66-6.45 (m, 2H), 5.94-5.89 (m, 1H), 4.2 9br, 1H), 3.76-2.92 (s overlaps m, 9H), 2.21-2.11 (m, 2H), 1.51-1.46 (br, 3H). LC-MS calcd for $\text{C}_{27}\text{H}_{26}\text{ClF}_3\text{N}_2\text{O}_6\text{S}_2$: 632. Observed : 633 (MH^+).

EXAMPLE 488

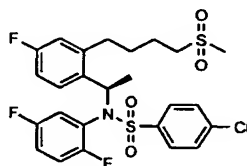
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(methylsulfanyl)butyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.33$ (9:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.67-7.57 (m, 2H), 7.43-7.37 (m, 2H), 7.02-6.312 (m, 6H), 5.86 (q, 1H), 3.1 (br, 1H), 2.70-2.59 (m, 3H), 2.14 (s, 3H), 1.77-1.75 (m, 4H), 1.55-1.53 (br, 3H). LC-MS calcd for $\text{C}_{25}\text{H}_{25}\text{ClF}_3\text{NO}_2\text{S}_2$: 528. Observed : 225 ($\text{M}^+ - 303$).

EXAMPLE 489

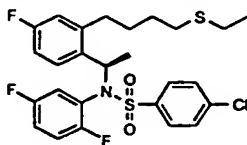
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(methylsulfonyl)butyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.52$ (1:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.70-7.62 (m, 2H), 7.49-7.38 (m, 2H), 7.02-6.24 (m, 6H), 5.88 (q, 1H), 3.30-3.07 (m, 3H), 2.96 (s, 3H), 2.88-2.70 (m, 1H), 2.10-1.86 (m, 4H), 1.52 (d, 3H). LC-MS calcd for $\text{C}_{25}\text{H}_{25}\text{ClF}_3\text{NO}_4\text{S}_2$: 560. Observed : 578 ($\text{M}^+ + \text{H}_2\text{O}$).

EXAMPLE 490

4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[4-(ethylsulfanyl)butyl]-4-fluorophenyl}ethyl)benzenesulfonamide



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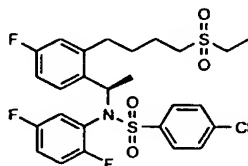
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$R_f = 0.33$ (9:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.68-7.58 (m, 2H), 7.45-7.38 (m, 2H), 6.99-6.31 (m, 6H), 5.85 (q, 1H), 3.1 (br, 1H), 2.70-2.61 (m, 3H), 2.57 (q, 2H), 1.78-1.73 (m, 2H), 1.53 (br, 3H), 1.28 (t, 3H). LC-MS calcd for $\text{C}_{26}\text{H}_{27}\text{ClF}_3\text{NO}_2\text{S}_2$: 542. Observed : 239 ($\text{M}^+ - 303$).

EXAMPLE 491

4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[4-(ethylsulfonyl)butyl]-4-fluorophenyl}ethyl)benzenesulfonamide



$R_f = 0.14$ (3:1;hexanes:ethyl acetate). ^1H NMR (CDCl_3) δ (ppm): 7.71-7.63 (m, 2H), 7.48-7.36 (m, 2H), 7.02-6.31 (m, 6H), 5.87 (q, 1H), 3.31-3.22 (m, 3H), 3.06 (q, 2H), 2.17-1.67 (m, 4H), 1.48 (d, 3H), 1.41 (t, 3H). LC-MS calcd for $\text{C}_{26}\text{H}_{27}\text{ClF}_3\text{NO}_4\text{S}_2$: 574. Observed : 592 ($\text{M}^+ + \text{H}_2\text{O}$).

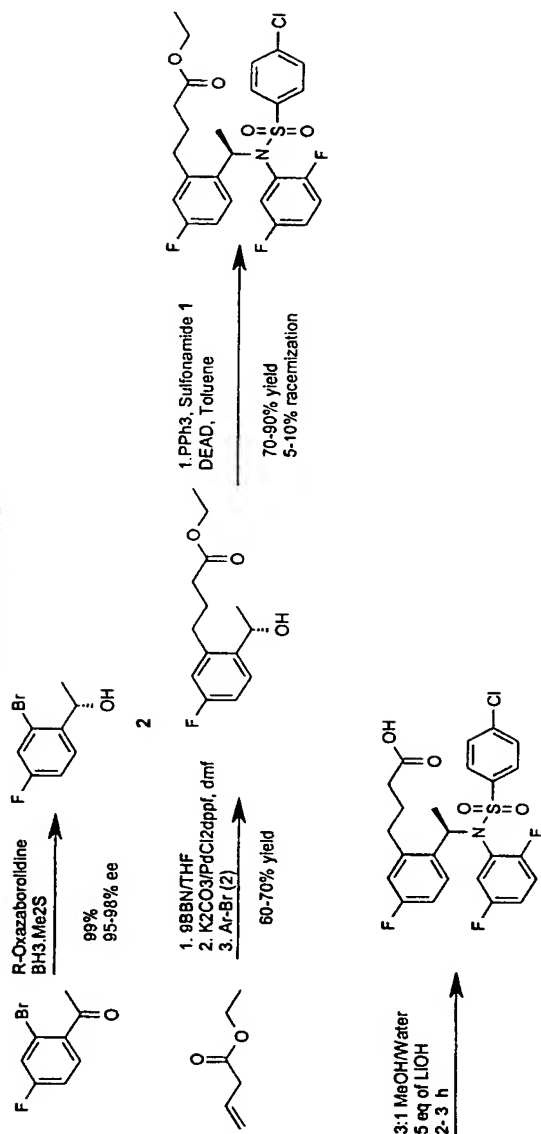
EXAMPLE 492

Numerous compounds according to the invention can be prepared employing the general scheme set forth in SCHEME 492.

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SCHEME 492

In an oven-dried two necked 100 mL round bottom flask under a vigorous stream of Ar was placed a solution of (*R*)- Oxazaborolidine in toluene (5.5 mL 1.27 M, 7 mmol, Strem) . To this solution was slowly added $\text{BH}_3\cdot\text{Me}_2\text{S}$ solution (8.3 mL, 83 mmol, 10.0 M, Aldrich). The reaction mixture was then cooled to -20°C and neat ketone (30.0 g, 138 mmol, Marshalton) was added through a syringe pump over a period of 4-5 h while keeping the bath temperature at -20°C . After the addition was complete the reaction mixture was allowed to stir at -20°C until the reaction was complete by GC (about 2 h). The reaction mixture was then carefully quenched by adding to pre-cooled methanol (-20°C .) and stirred for 1 h. The reaction mixture was then concentrated under reduced pressure and the crude product was purified by filtration through silica gel by eluting with 10:1-6:1 hexanes:ethyl acetate to separate the product from the catalyst. Isolated quantitative yield of the product. R_f (10:1 hexanes:ethyl acetate) 0.32. ^1H NMR (CDCl_3) δ 7.60-7.57 (dd, 1H), 7.27-7.31 (m, 2H), 7.10-7.00 (m, 1H), 5.30-5.17 (dq, 1H), 1.99 (s, 1H), 1.49 (d, 3H).

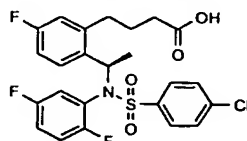
Ethyl vinylacetate (27.98 g, 218.3 mmol) was dissolved in 100 mL of dry THF, in an oven dried flask. The flask was cooled in an ice bath and a solution of 9-BBN (0.5 M, 437mL, 218.5 mmol, Aldrich) was added over a period of 1 h. The reaction mixture was allowed to stir at room temperature for 8 h and then added K_2CO_3 (70.0 g, 506 mmol), DMF (700 mL), alcohol (40 g, 182 mmol) and PdCl_2dppf (4.0 g, 2.7 mol%, Aldrich). The reaction mixture was heated to 60°C for 21 h at which time TLC shows complete consumption of the alcohol. The reaction mixture was then cooled to room temperature, filtered through celite and concentrated. The crude reaction mixture was purified by chromatography over SiO_2 (1 .0 Kg of SiO_2 , 5:1 hexanes:ethyl acetate) to isolate 37 g of pale yellow oil (95 % pure). ^1H NMR (CDCl_3) δ 7.52-7.50 (dd, 1H), 6.96-6.82 (m, 3H), 5.15-5.11 (br q, 1H), 4.13-4.06 (q, 2H), 2.75-2.63 (m, 2H), 2.35 (t, 2H), 1.93 (p, 2H), 1.48 (d, 3H), 1.23 (t, 3H).

EXAMPLE 493

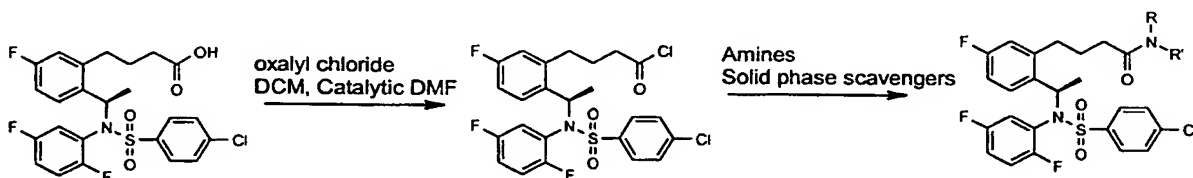
ethyl 4-[2-((1*R*)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]butanoate

To a solution of PPh_3 (41.2 g, 157 mmol, Aldrich), in 180 mL of dry toluene was added solid sulfonamide 1 (47.6 g, 157 mmol). The solution was stirred at room temperature for 30 min (sulfonamide dissolves only partially) and cooled to 0°C in an ice-bath. Neat DEAD (24.7 mL, 157 mmol, Aldrich) was slowly added to the reaction mixture. The sulfonamide dissolves as the addition of DEAD progresses. After the addition was over, the reaction mixture was allowed to warm to room temperature and a solution of the alcohol (37 g, 131 mmol) in 80 mL of dry toluene was added through a syringe pump over a period of 5 h. The reaction mixture was then allowed to stir at room temperature until TLC shows complete consumption of starting material (21 h). The reaction mixture was then concentrated under reduced pressure. The phosphine oxide was crystallized from 6:1 hexanes:ethyl acetate and the mother liquor was concentrated and purified by chromatography (7:1 hexanes:ethyl

acetate) to isolate 51 g of product as pale yellow oil. R_f (10:1 hexanes:ethyl acetate) 0.33 ^1H NMR (CDCl_3) δ 7.65-7.58 (m, 2H), 7.41-7.39 (m, 2H), 7.15-6.31 (m, 6H), 5.82 (q, 1H), 4.16 (q, 2H), 3.10 (m, 1H), 2.68 (m, 1H), 2.4 (t, 2H), 1.93 (m, 2H), 1.52-1.45 (br 3H), 1.45 (t, 3H).

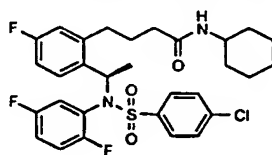
EXAMPLE 4945 **4-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]butanoic acid**

A solution of the ester (48 g, in 700 mL of methanol) was cooled to 0°C and 230 mL of LiOH solution (10.2 g of LiOH in 230 mL of water) was added slowly. The reaction mixture turned turbid, and a pale yellow precipitate separates. The reaction mixture was mechanically stirred at 0°C for 1 h and at room temperature for 2 h. The reaction mixture was then cooled to 0°C and carefully adjusted to pH 1 with 6 N HCl. Extracted the product with 4 x 250 mL of ethyl acetate, washed the ethyl acetate solution with dilute brine (3 x 200 mL), dried the organic layer with MgSO_4 , filtered and concentrated to yield crude product. The crude product was purified by SiO_2 chromatography (1:1 hexanes:ethyl acetate) and the product was recrystallized from 4:1 hexanes:ethyl acetate (10 mL/g) to >98% ee. R_f (10:4 hexanes:ethyl acetate) 0.15. ^1H NMR (CDCl_3) δ 6.66-7.59 (m, 2H), 7.43-7.40 (m, 2H), 6.99-6.33 (m, 6H), 5.85 (q, 1H), 3.15-3.11 (m, 1H), 2.78-2.68 (m, 1H), 2.54 (t, 2H), 2.02 (m, 2H), 1.54-1.52 (br d, 3H).

EXAMPLE 495

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Using the scheme outlined in the preparative scheme in this example, the of Examples 496-503 compounds were prepared.

EXAMPLE 49625 **4-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-cyclohexylbutanamide**

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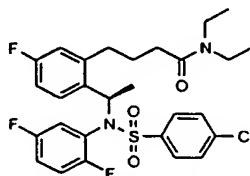
PCT/US00/04560

$R_f = 0.39$ (2:1 hexanes:ethyl acetate) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.70-7.59 (m, 2H), 7.47-7.41 (m, 2H), 7.01-6.32 (m, 6H), 5.92-5.85 (q, 1H), 5.62 (br, 1H), 3.86-3.74 (m, 1H), 3.12-3.03 (m, 1H), 2.80-2.70 (m, 1H), 2.38-2.28 (m, 2H), 2.01-1.92 (br, 4H), 1.73-1.07 (m, 11H). LC-MS calculated for $\text{C}_{30}\text{H}_{32}\text{ClF}_3\text{N}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 593; Observed: 290 ($\text{MH}^+ - 303$).

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EXAMPLE 497

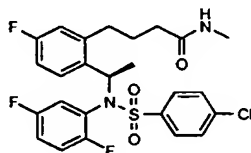
4-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N,N-diethylbutanamide



$R_f = 0.35$ (2:1 hexanes:ethyl acetate) ^1H NMR (300MHz CDCl_3) δ (ppm) : 7.70-7.61 (m, 2H), 7.45-7.43 (br, 2H), 7.00-6.32 (br, 6H), 5.93-5.87 (q, 1H), 3.46-3.32 (m, 4H), 3.18-3.11 (m, 1H), 2.75-2.70 (m, 1H), 2.51-2.46 (t, 2H) 2.05-1.95 (m, 2H), 1.51-1.49 (br, 3H), 1.26-1.12 (m, 6H). LC-MS calculated for $\text{C}_{28}\text{H}_{30}\text{ClF}_3\text{N}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 567; Observed: 567.

EXAMPLE 498

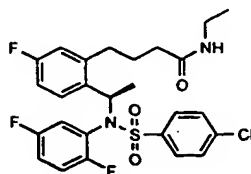
4-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-methylbutanamide



$R_f = 0.17$ (1:1 hexanes:ethyl acetate) ^1H NMR (300MHz CDCl_3) δ : 7.71-7.60 (m, 2H), 7.48-7.41 (m, 2H), 7.00-6.30 (m, 6H), 5.93-5.86 (q, 1H), 5.80 (br, 1H), 3.13-3.03 (m, 1H), 2.85-2.74 (m, 4H), 2.40-2.35 (t, 2H), 2.02 (br, 2H), 1.50-1.47 (br, 3H). LC-MS calculated for $\text{C}_{25}\text{H}_{24}\text{ClF}_3\text{N}_2\text{O}_3\text{S}$ $[\text{MH}^+]$ 525; Observed: MH-303.

EXAMPLE 499

4-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-ethylbutanamide



$R_f = 0.31$ (1:1 hexanes:ethyl acetate) ^1H NMR (300MHz CDCl_3) δ : 7.70-7.60 (m, 2H), 7.48-7.41 (m, 2H), 7.00-6.31 (m, 6H), 5.93-5.86 (q, 1H), 5.73 (br, 1H), 3.38-3.28 (m, 2H), 3.13-3.03 (m,

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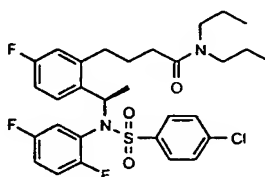
248

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1H), 2.78-2.73 (m, 1H), 2.38-2.33 (t, 2H), 2.02-2.01 (br, 2H), 1.50-1.47 (br, 3H), 1.18-1.13 (t, 3H).
LC-MS calculated for C₂₆H₂₆ClF₃N₂O₃S [MH⁺] 539; Observed: MH-303.

EXAMPLE 500

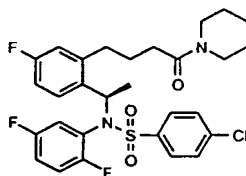
4-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N,N-dipropylbutanamide



R_f = 0.46 (3:1 hexanes:ethyl acetate) ¹H NMR (300MHz CDCl₃) δ: 7.70-7.61 (m, 2H), 7.45-7.43 (m, 2H), 7.00-6.31 (m, 6H), 5.93-5.86 (q, 1H), 3.34-3.11 (m, 5H), 2.75-2.70 (m, 1H), 2.51-2.46 (t, 2H), 2.04-1.97 (m, 2H), 1.65-1.49 (m, 7H), 0.95-0.88 (m, 6H). LC-MS calculated for C₃₀H₃₄ClF₃N₂O₃S [MH⁺] 595; Observed: 595.

EXAMPLE 501

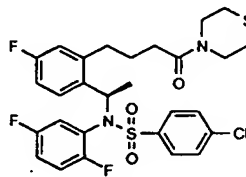
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-oxo-4-(1-piperidinyl)butyl]phenyl}ethyl)benzenesulfonamide



R_f = 0.31 (2:1 hexanes:ethyl acetate) ¹H NMR (300MHz CDCl₃) δ: 7.70-7.60 (m, 2H), 7.46-7.43 (m, 2H), 7.00-6.32 (m, 6H), 5.92-5.85 (q, 1H), 3.62-3.58 (t, 2H), 3.47-3.43 (t, 2H), 3.15-3.11 (m, 1H), 2.78-2.68 (m, 1H), 2.52-2.47 (t, 2H), 2.03-1.93 (m, 2H), 1.66-1.49 (m, 9H). LC-MS calculated for C₂₉H₃₀ClF₃N₂O₃S [MH⁺] 579; Observed: 579.

EXAMPLE 502

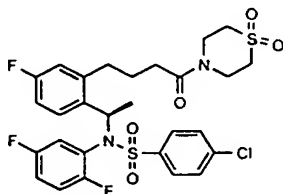
4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-oxo-4-(4-thiomorpholinyl)butyl]phenyl}ethyl)benzenesulfonamide



R_f = 0.38 (2:1 hexanes:ethyl acetate) ¹H NMR (300MHz CDCl₃) δ: 7.70-7.60 (m, 2H), 7.47-7.40 (m, 2H), 7.01-6.31 (m, 6H), 5.94-5.87 (q, 1H), 3.94-3.91 (t, 2H), 3.81-3.78 (t, 2H), 3.12-3.10 (m, 1H), 2.84-2.71 (m, 1H), 2.65-2.64 (br, 4H), 2.53-2.49 (t, 2H), 2.06-1.96 (m, 2H), 1.49-1.47 (br, 3H). LC-MS calculated for C₂₈H₂₈ClF₃N₂O₃S₂ [MH⁺] 597, Observed 597.

EXAMPLE 503

4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(4-thiomorpholinylsulfonyl)butyl]phenyl}ethyl)benzenesulfonamide



$R_f = 0.46$ (1:1 hexanes:ethyl acetate) ^1H NMR (300MHz CDCl_3) δ : 7.71-7.59 (m, 2H), 7.51-7.41 (m, 2H), 7.07-6.29 (m, 6H), 5.96-5.94 (br, 1H), 4.14-4.04 (d, 4H), 3.07-2.83 (m, 6H), 2.64-2.59 (t, 2H), 2.08-2.03 (m, 2H), 1.44-1.42 (d, 3H). LC-MS calculated for $\text{C}_{28}\text{H}_{28}\text{ClF}_3\text{N}_2\text{O}_5\text{S}_2$ $[\text{MH}^+]$ 629; Observed: MH-303.

EXAMPLE 504**General Procedure for the synthesis of amine oxides**

The free base (0.5g) was dissolved in methanol (5 mL) and 30% H_2O_2 in water (5 mL) was added. The mixture was stirred at room temperature for 14 h then concentrated under reduced pressure. The resulting crude product was purified by chromatography on SiO_2 to yield the desired *N*-oxide product in >90% yield.

Using the preparative scheme described in the previous example, the following compounds were prepared.

EXAMPLE 505

4-chloro-N-{2-[3-(1-hydroxy-1 λ 5-piperidin-1-yl)propoxy]benzyl}-N-phenylbenzenesulfonamide

$R_f = 0.15$ (1% triethylamine/5% methanol/ethyl acetate) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.55 (m, 4H), 7.21 (m, 4H), 6.78 (m, 4H), 6.60 (m, 1H), 4.74 (s, 2H), 4.53 (m, 2H), 4.19 (m, 4H), 3.53 (t, 2H), 2.67 (m, 2H), 2.35 (m, 2H), 1.87-1.27 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 156.9, 139.6, 137.2, 136.0, 131.9, 130.1, 129.4, 129.0, 128.9, 128.8, 128.5, 121.5, 120.2, 110.7, 66.5, 64.6, 63.6, 51.3, 29.7, 22.1, 21.3, 20.3. ESI calculated for $\text{C}_{27}\text{H}_{31}\text{ClN}_2\text{O}_4\text{S}$ $[\text{MH}^+]$ 515; Observed: 515.

EXAMPLE 506

4-chloro-N-(2,5-dichlorophenyl)-N-{2-[3-(1-oxido-1-piperidinyl)propoxy]benzyl}benzenesulfonamide

$R_f = 0.42$ (10% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.64-7.51 (m, 4H), 7.26-7.14 (m, 4H), 6.81-6.03 (m, 3H), 4.97-4.80 (dd, 2H), 4.47-4.17 (m, 6H), 3.45 (m, 2H), 2.64 (m, 2H), 2.28 (m, 2H), 1.86 (m, 3H), 1.49 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 157.3, 140.3, 137.3, 135.8, 134.1, 132.8, 132.4, 131.8, 131.6, 131.0, 130.5, 129.9, 129.3, 121.2, 120.8, 111.2, 66.9, 65.1, 64.6, 63.5, 50.42, 22.5, 21.6, 20.7.

EXAMPLE 507**4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-oxido-1-pyrrolidiny)propoxy]benzyl}benzenesulfonamide**

$R_f = 0.38$ (9% methanol/DCM) ^1H NMR (500 MHz, CD_3OD) δ (ppm): 7.69-7.61 (m, 4H), 7.18 (m, 1H), 7.01-6.89 (m, 4H), 6.77-6.67 (m, 2H), 4.13 (t, 2H), 3.81 (m, 2H), 3.64-3.48 (m, 4H), 2.52-2.33 (m, 4H), 2.09 (m, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ (ppm): 160.4, 159.1, 158.7, 158.4, 157.1, 140.9, 138.5, 132.8, 131.4, 130.8, 130.5, 127.6, 123.5, 121.4, 120.1, 119.9, 118.5, 118.4, 118.4, 118.3, 118.2, 118.1, 112.3, 69.1, 66.8, 66.4, 51.0, 25.6, 22.7. ESI calculated for $\text{C}_{26}\text{H}_{27}\text{ClF}_2\text{N}_2\text{O}_4\text{S}$ $[\text{MH}^+]$ 537; Observed: 537.

EXAMPLE 508**4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1,1,4-trioxido-4-thiomorpholinyl)propoxy]benzyl}benzenesulfonamide**

$R_f = 0.53$ (9% methanol/DCM) ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.65-7.48 (m, 4H), 7.32-7.16 (m, 1H), 6.91-6.58 (m, 6H), 4.78 (s, 2H), 4.39-3.92 (m, 8H), 3.65 (m, 2H), 2.96 (m, 2H), 2.64 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 159.3, 157.9, 156.9, 156.1, 154.5, 139.7, 136.6, 131.4, 130.3, 129.4, 128.7, 125.7, 125.6, 125.4, 121.5, 120.4, 118.9, 118.5, 117.2, 117.1, 117.0, 116.9, 116.8, 116.7, 110.8, 69.4, 65.5, 63.4, 50.0, 46.3, 23.0. ESI calculated for $\text{C}_{26}\text{H}_{27}\text{ClF}_2\text{O}_6\text{S}_2\text{N}_2$ $[\text{MH}^+]$ 601; Observed: 601.

EXAMPLE 509**4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-oxido-1-piperidiny)propoxy]benzyl}benzenesulfonamide**

$R_f = 0.45$ (9% methanol/DCM) ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.68-7.54 (m, 4H), 7.23-6.67 (m, 6H), 6.29-6.22 (m, 2H), 4.26 (m, 2H), 3.70-3.48 (m, 4H), 3.06 (m, 2H), 2.41 (m, 2H), 2.01-1.51 (m, 9H). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 158.9 (dd), 157.2, 155.6 (dd), 140.2, 137.0, 131.8, 130.8, 129.9, 129.1, 125.7 (dd), 121.5, 120.7, 118.8 (d), 117.7 (t), 11.4 (t), 111.2, 66.8, 65.0, 64.5, 50.6, 22.5, 21.6, 20.7. ESI calculated for $\text{C}_{27}\text{H}_{29}\text{ClF}_2\text{N}_2\text{O}_4\text{S}$ $[\text{MH}^+]$ 551; Observed: 551.

EXAMPLE 510**4-chloro-N-{2-[3-(diethylnitroxy)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide**

$R_f = 0.49$ (9 % methanol in DCM), ^1H NMR (300 MHz, CD_3OD) δ (ppm) (d, 2H), 7.61 (d, 2H), 7.19 (t, 1H), 7.02-6.99 (m, 2H), 6.95 (d, 1H), 6.89 (d, 1H), 6.78-6.70 (m, 2H), 4.83 (s, 2H), 4.12 (t, 2H), 3.69-3.66 (m, 2H), 3.44-3.40 (m, 4H), 2.37-2.34 (m, 2H), 1.37 (t, 6H). MS calculated for $\text{C}_{26}\text{H}_{29}\text{ClF}_2\text{N}_2\text{O}_4\text{S}$: 539; Observed: 539.

EXAMPLE 511**General Procedure for the synthesis of quaternary ammonium compounds**

The free base was dissolved in DCM (2 mL/mmol) and excess of MeI (4.0 eq) was added. The reaction mixture was stirred at room temperature for 1 h then concentrated under reduced pressure to give pure quaternary ammonium compounds.

EXAMPLE 512**1-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-1-methylpiperidinium iodide**

$R_f = 0.42$ (3:1:1 n-BuOH/H₂O/AcOH) ¹H NMR (300 MHz, CD₃OD) δ (ppm): 7.69-7.57 (m, 4H), 7.18-6.59 (m, 7H), 4.80 (s, 2H), 4.16 (t, 2H), 3.88 (m, 2H), 3.59 (m, 4H), 3.18 (s, 2H), 2.37 (m, 2H), 1.93-1.60 (m, 6H).

EXAMPLE 513**1-{3-[2-({[2,5-dichloro[(4-chlorophenyl)sulfonyl]anilino)methyl}phenoxy]propyl}-1-methylpiperidinium iodide**

$R_f = 0.32$ (10:1;DCM:methanol). ¹H NMR (300 MHz, CD₃OD) δ (ppm):7.74-7.63 (m, 4H), 7.28-7.18 (m, 3H), 6.93 (d,1H), 6.86 (d, 1H), 6.75 (dd, 1H), 6.64 (dt, 1H), 5.13 (d, 1H), 4.67 (d, 1H), 4.27-4.26 (m, 1H), 4.11-4.02 (m, 2H), 3.86-3.79 (m, 1H), 3.52 (br m, 4H), 3.22 9s, 3H), 2.40- (br m, 2H), 1.99-1.64 (m, 6H). MS ESI calculated for C₂₈H₃₂Cl₃N₂O₃S: 581. Observed : 581.

EXAMPLE 514

Compounds of the present invention can be prepared using the following general schemes.

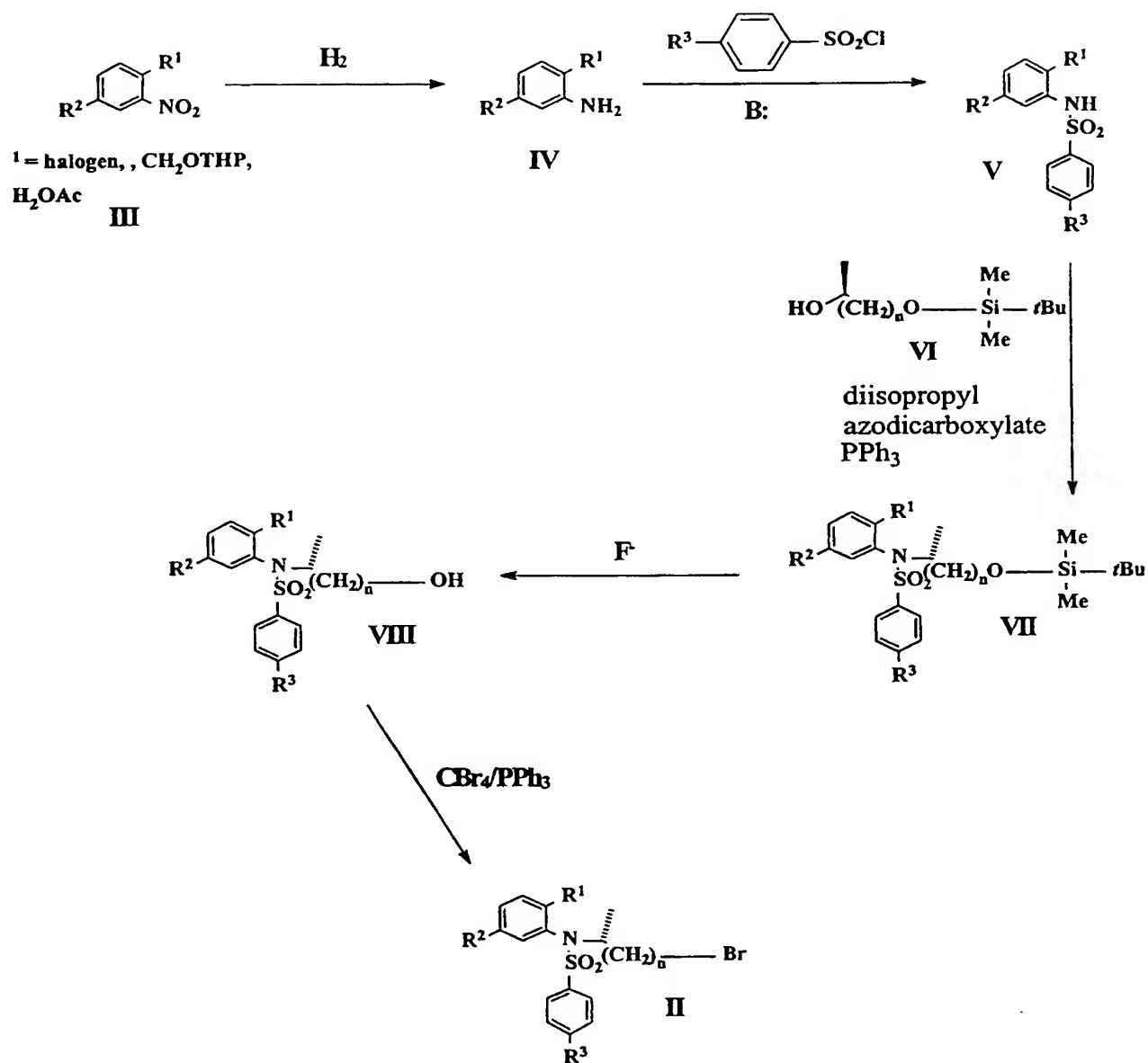
In Schemes 514a, 514b and 514c, R¹ is halogen, methyloxytetrahydropyranyl, or a methyloxyacyl moiety such as -CH₂OAc. R² is hydrogen or halogen; R³ is hydrogen, halogen or substituted or unsubstituted alkyl; R⁴ and R⁵ are substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, alkoxy, ether, ester, amide, R⁶ is substituted or unsubstituted hydrocarbyl, or substituted or unsubstituted heterocycle optionally having one or more double bonds; n is an integer from 1 up to 4, and Z is heterocycle optionally having one or more double bonds.

Scheme 514a illustrates a general process and shows the production of chiral compounds of a key intermediate of Formula II.

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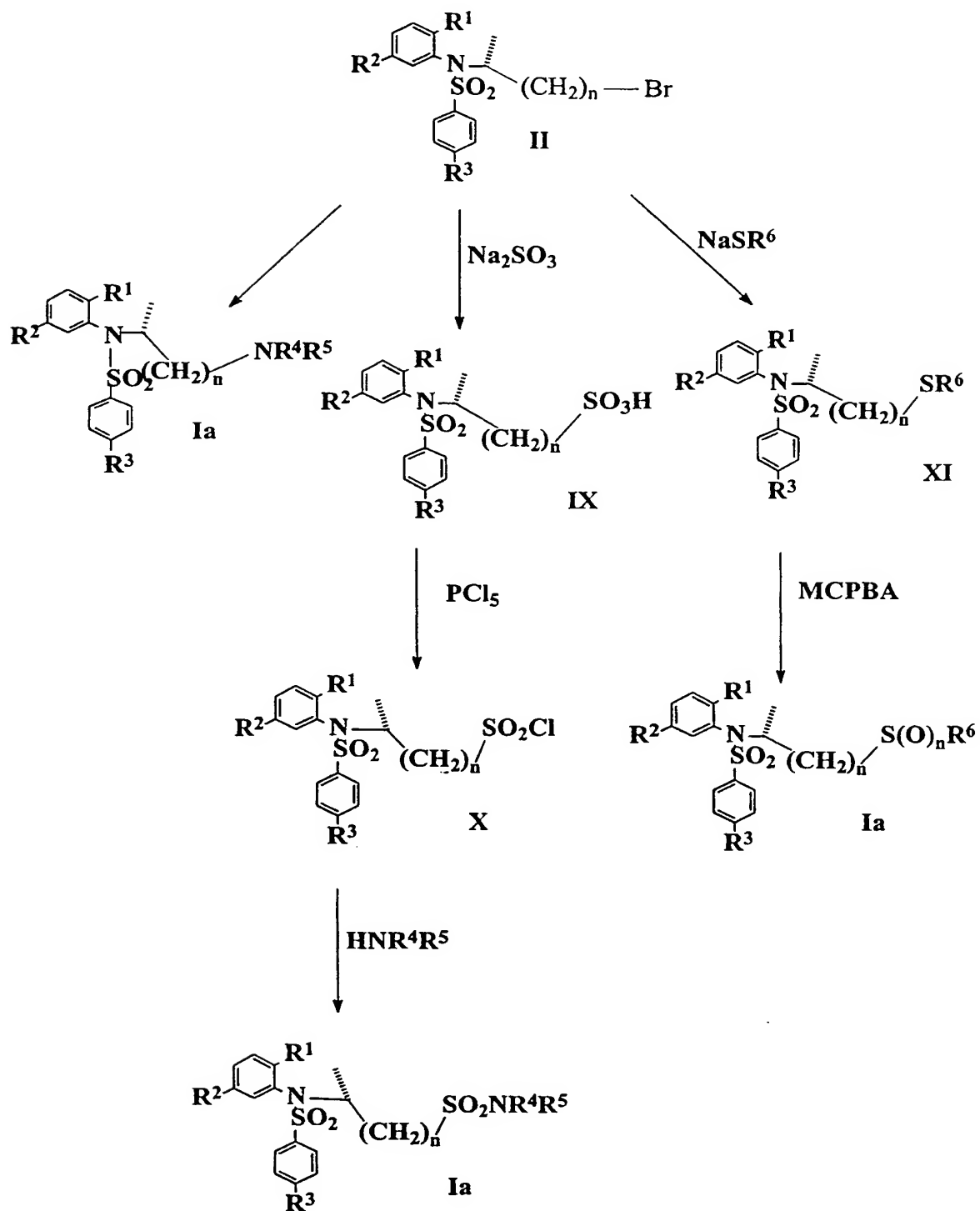
PCT/US00/04560

252

Scheme 514a**Synthesis of Intermediate II**

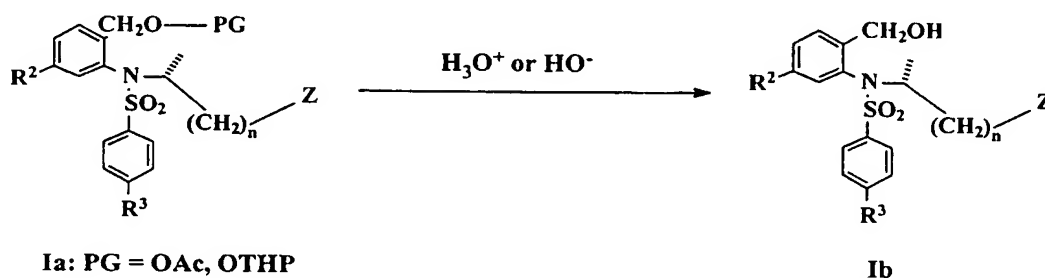
The Scheme 514a process begins with reduction of 2,5-disubstituted-nitrobenzene (III) to the corresponding substituted aniline (IV) which is reacted with an R³-substituted benzenesulfonyl halide to provide intermediate (V). Treatment of (V) with (S)-4-[[dimethyl(1,1-dimethylethyl)silyl]oxy]-2-alkan-5-ol gives compound VII which is converted, in turn, to the corresponding alcohol (VIII) and then to the halide (II) with bromide being the preferred halide.

Scheme 514b illustrates several methods of producing some of the Formula I products; i.e., when R¹ is halogen, -CH₂O-2-tetrahydropyran or -CH₂OAc.

Scheme 514b**Preparation of Formula Ia Products**

In Scheme 514b, products (Ia) can be obtained starting with intermediate compound (II). Products (Ia) can be formed directly from intermediate compound (II) by reaction with nucleophilic heterocyclics. Alternatively, intermediate compound (II) can be converted into compounds (X and XI), which can then be used to produce products (Ia) as shown in Scheme 2.

5 Scheme 514c shows preparation of Formula I products wherein R^1 is $-\text{CH}_2\text{OH}$.

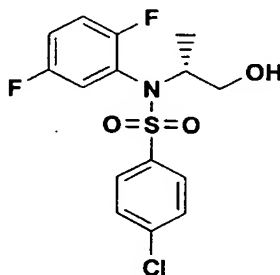


In Scheme 514c, cleavage of acetyl or tetrahydropyran groups from compounds of Formula Ia provide Formula Ib products wherein R^1 is $-\text{CH}_2\text{OH}$.

EXAMPLE 515

10 In the following examples, intermediate alcohols were prepared via a Mitsunobu reaction between a secondary sulfonamide and a commercially available TBDMS protected chiral diol, followed by HF deprotection as described herein.

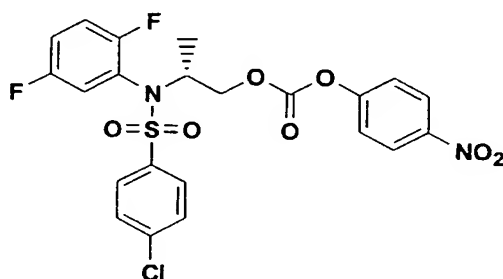
4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-2-hydroxyethyl]benzenesulfonamide



15 Yield=70%; Colorless viscous oil: IR (neat, CH_2Cl_2) 1504, 1346, 1164, 1093, 755, 625 cm^{-1} ; MS (ESI+), 362 ($\text{M}+\text{H}$) $^+$.

EXAMPLE 516

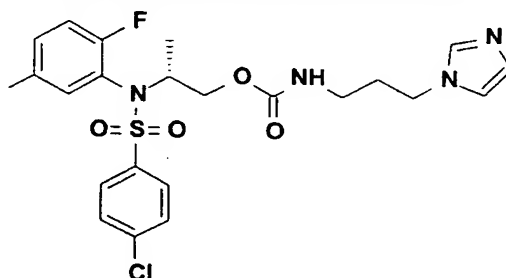
4-chloro-N-(2,5-difluorophenyl)-N-[2-[[[4-nitrophenyl]oxy]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



- 5 To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[(R)-1-methyl-2-hydroxyethyl] benzenesulfonamide (958 mg, 2.65 mmol) in THF (13 mL) and acetonitrile (2 ml) was added pyridine (209 mg, 2.65 mmol) followed by 4-nitrophenyl chloroformate (586 mg, 2.92 mmol). The resulting mixture was allowed to stir at 22°C for 16 h. The solvents were removed and the product was dissolved in ether, washed with water, then brine. The ether layer was dried over MgSO₄, filtered, and
- 10 concentrated under reduced pressure. Silica gel chromatography (ethyl acetate:hexane, 5-20% ethyl acetate gradient) of the concentrate afforded the title compound (1.23 g, yield 88%) as a colorless viscous oil.

EXAMPLE 517

4-chloro-N-(2,5-difluorophenyl)-N-[2-[[N'-[3-(1H-imidazol-1-yl)propylamino] carbonyl]oxy]-(r)-1-methylethyl]benzenesulfonamide

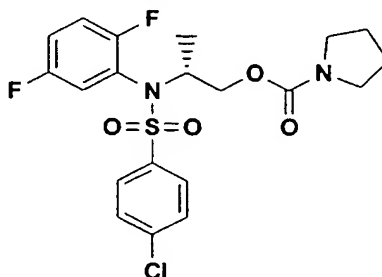


- 15 To a solution of 4-chloro-N-(2,5-difluorophenyl)-N-[2-[[[4-nitrophenyl]oxy]carbonyl] oxy]-1(R)-methylethyl]benzenesulfonamide (580 mg, 1.10 mmol) in methanol (5 ml) was added 3-aminopropyl-(1H)-imidazole (276mg, 2.20 mmol). The resulting mixture was allowed to stir at 22°C
- 20 for 16 h, then concentrated under reduced pressure. Silica gel chromatography (methanol in CH₂Cl₂ with 0.5% NH₄OH, 5-10% methanol gradient) of the concentrate afforded the title compound (344 mg, 61%) as a pale yellow powder. IR (KBr) 1722, 1506, 1345, 1261, 1183, 623 cm⁻¹; MS (ESI+), 513 (M+H)⁺.

Non basic carbamates shown in the following examples were prepared in an analogous manner as described above but were purified via silica gel chromatography (ethyl acetate:hexane 5-50% ethyl acetate gradient) of the concentrate.

EXAMPLE 518

5 **4-chloro-N-(2,5-difluorophenyl)-N-[2-[[[pyrrolidin-1-yl] carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide**

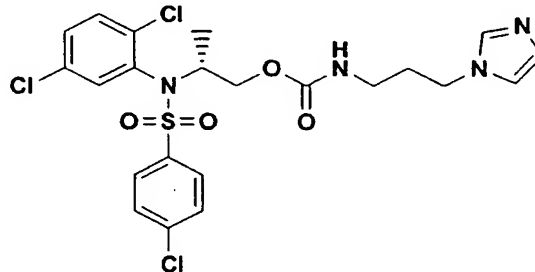


Yield=87%; Colorless viscous oil: IR (neat, CH₂Cl₂) 1704, 1504, 1424, 1352, 1165, 1092 cm⁻¹; MS (ESI+), 459 (M+H)⁺.

10

EXAMPLE 519

4-chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-(3-(1H-imidazol-1-yl)propylamino] carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

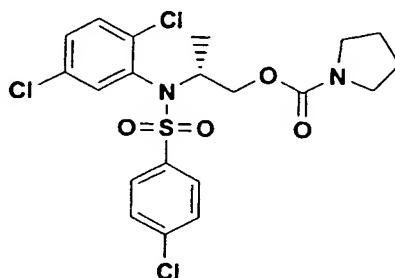


Yield=81%; pale yellow powder: IR (neat, CH₂Cl₂) 1718, 1467, 1250, 1169, 1085, 622 cm⁻¹;

15 MS (ESI+), 545 (M+H)⁺.

EXAMPLE 520

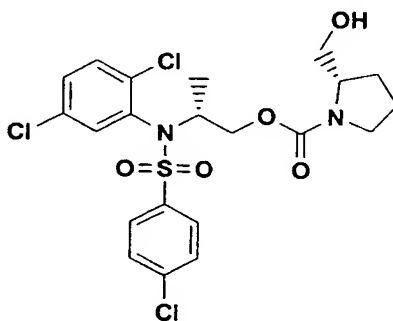
4-chloro-N-(2,5-dichlorophenyl)-N-[2-[[[pyrrolidin-1-yl]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



5 Yield=81%; White solid: IR (KBr) 1702, 1430, 1352, 1174, 1099, 620 cm^{-1} ; MS (ESI+), 491 (M+H)⁺.

EXAMPLE 521

4-chloro-N-(2,5-dichlorophenyl)-N-[2-[[[(S)-2-(hydroxymethyl)pyrrolidin-1-yl]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

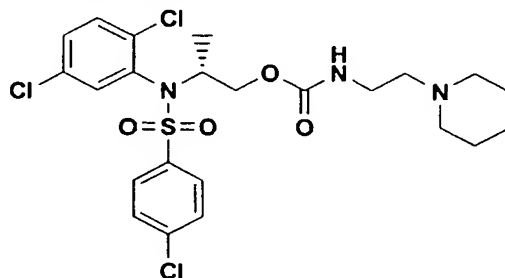


10

Yield=81%; Colorless glassine solid: IR (KBr) 1699, 1421, 1356, 1170, 1095, 622 cm^{-1} ; MS (ESI+), 521 (M+H)⁺.

EXAMPLE 522

4-chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-(2-(piperidin-1-yl)ethylamino) carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

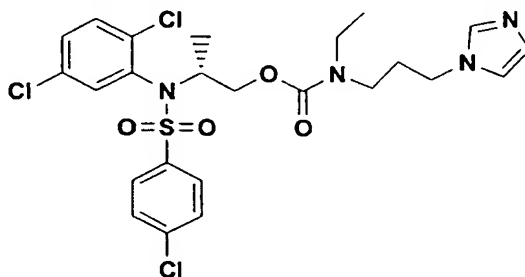


5

Yield=73%; Colorless glassine solid: IR (neat, CH₂Cl₂) 1723, 1468, 1352, 1170, 1095, 622 cm⁻¹; MS (ESI+), 548 (M+H)⁺.

EXAMPLE 523

4-chloro-N-(2,5-dichlorophenyl)-N-[2-[[[N'-(3-(1H-imidazol-1-yl)propyl)-N'-ethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

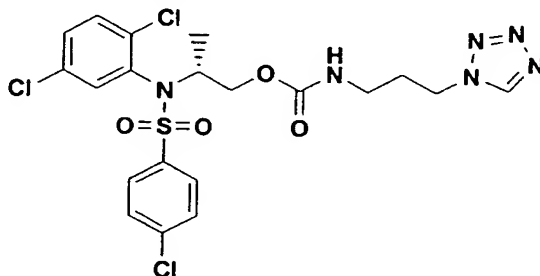


10

Yield=48%; Pale yellow viscous oil: IR (neat, CH₂Cl₂) 1699, 1467, 1352, 1170, 1095, 623 cm⁻¹; MS (ESI+), 573 (M+H)⁺.

EXAMPLE 524

4-chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-[3-(1H-tetrazol-1-yl)-propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

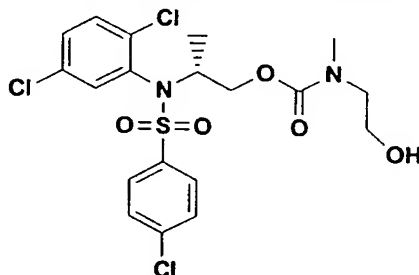


5

Yield=46%; White powder: IR (KBr) 1718, 1467, 1348, 1168, 1095, 622 cm^{-1} ; MS (ESI+), 547 (M+H)⁺.

EXAMPLE 525

4-chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-[2-(hydroxyethyl)-N'-methylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

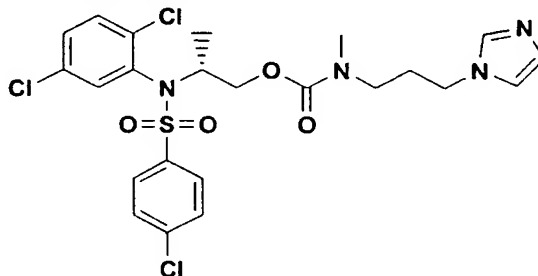


10

Yield=80%; Pale yellow viscous oil: IR (neat, CH₂Cl₂) 1699, 1466, 1354, 1170, 1095, 623 cm⁻¹; MS (ESI+), 495 (M+H)⁺.

EXAMPLE 526

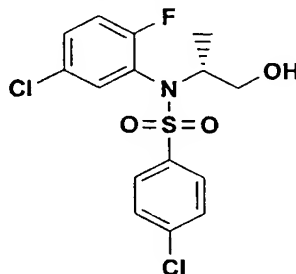
4-chloro-N-(2,5-dichlorophenyl)-N-[2-[[[N'-[3-(1H-imidazol-1-yl)propyl]-N'-methylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



Yield=50%; Pale yellow gummy solid: IR (neat, CH₂Cl₂) 1699, 1467, 1352, 1170, 1095, 622 cm⁻¹; MS (ESI+), 559 (M+H)⁺.

EXAMPLE 527

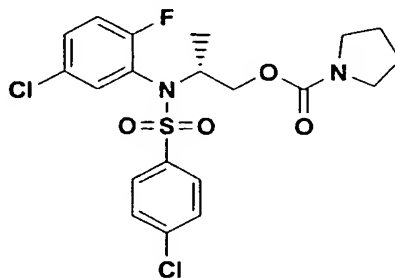
4-chloro-N-(2-fluoro-5-chlorophenyl)-N-[(R)-1-methyl-2-hydroxyethyl]benzenesulfonamide



Yield=83%; Colorless viscous oil: IR (neat, CH₂Cl₂) 1493, 1345, 1166, 1054, 758, 622 cm⁻¹; MS (ESI+), 378 (M+H)⁺.

EXAMPLE 528

4-chloro-N-(2-fluoro-5-chlorophenyl)-N-[2-[[[pyrrolidin-1-yl] carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

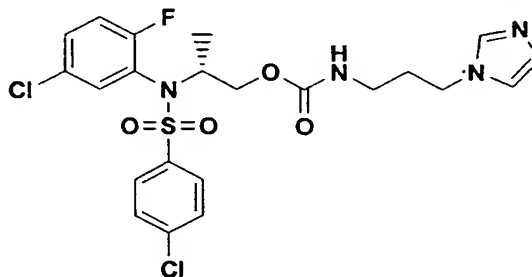


5

Yield=71%; White powder: IR (neat, CH₂Cl₂) 1704, 1494, 1424, 1352, 1171, 622 cm⁻¹; MS (ESI+), 475 (M+H)⁺.

EXAMPLE 529

4-chloro-N-(2-fluoro-5-chlorophenyl)-N-[2-[[N'-[3-(1H-imidazol-1-yl)propylamino] carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

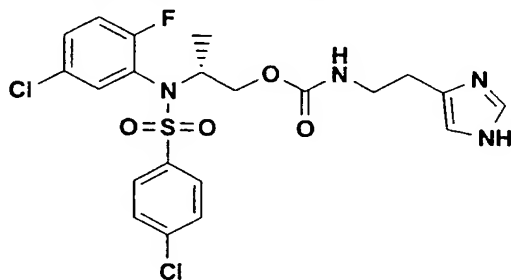


10

Yield=81%; White powder: IR (KBr) 1720, 1345, 1263, 1171, 758, 620 cm⁻¹; MS (ESI+), 529 (M+H)⁺

EXAMPLE 530

**4-chloro-N-(2-fluoro-5-chlorophenyl)-N-[2-[[N'-[2-(1H-imidazol-4-yl)ethylamino]carbonyl]oxy]-
(R)-1-methylethyl]benzenesulfonamide**

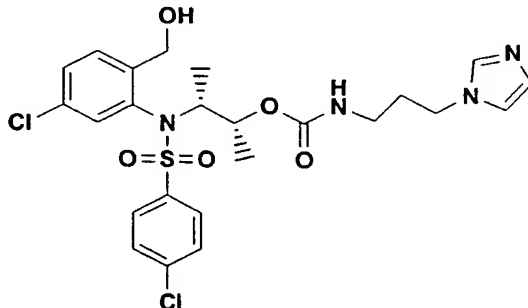


5

Yield=74%; White powder: IR (KBr) 1716, 1494, 1262, 1169, 1091, 758 cm^{-1} ; MS (ESI+), 515 (M+H)⁺.

EXAMPLE 531

4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[N'-[3-(1H-imidazol-1-yl)propylamino]carbonyl]oxy]-(1R)-(2R)-dimethylethyl]benzenesulfonamide

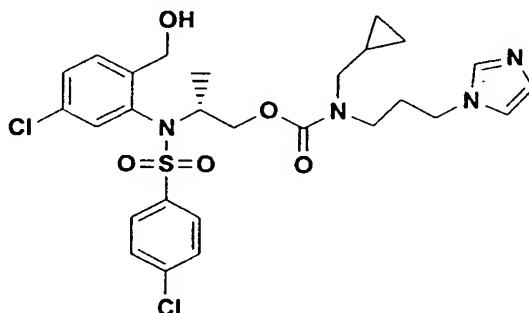


10

Yield=77%; White solid: IR (KBr) 1715, 1347, 1168, 1091, 757, 627 cm^{-1} ; MS (ESI+), 555 (M+H)⁺.

EXAMPLE 532

4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[N'-[3-(1H-imidazol-1-yl)propyl]-N'-cyclopropylmethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide.



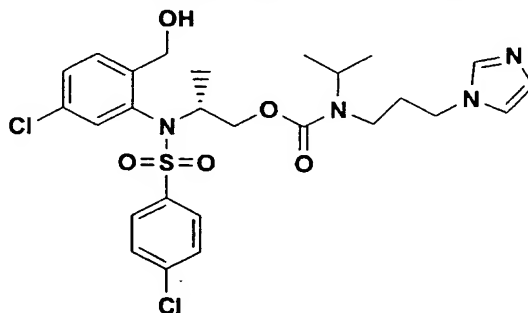
5

Yield=32%; Colorless glassine solid: IR (KBr) 1697, 1477, 1167, 1092, 758, 622 cm^{-1} ; MS (ESI+), 595 (M+H)⁺.

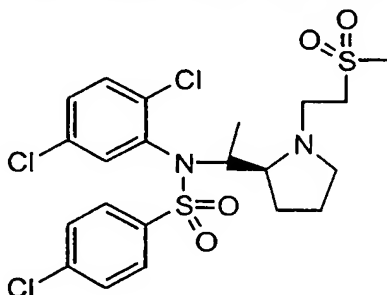
EXAMPLE 533

4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[N'-[3-(1H-imidazol-1-yl)propyl]-N'-(2-methylethyl)amino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

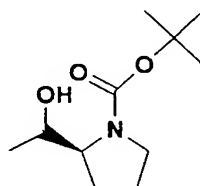
10



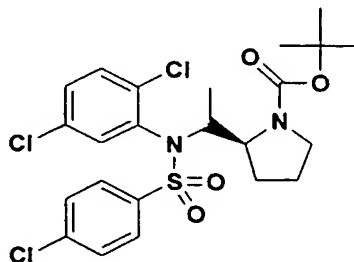
Yield=43%; Beige solid: IR (neat, CH_2Cl_2) 1342, 1166, 1092, 1055, 757, 622 cm^{-1} ; MS (ESI+), 583 (M+H)⁺.

EXAMPLE 534**4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-[1-[2-(methylsulfonyl)ethyl] pyrrolidin-2-yl]ethyl]benzenesulfonamide**

5 The above-named compound was prepared using the preparative scheme described below.

 α -methyl-[N-(*tert*-butoxycarbonyl)]-L-prolinol

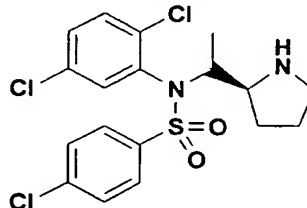
To a solution of (S)-2-acetyl-1-pyrrolidinecarboxylic acid 1,1-dimethylethyl ester [CA 91550-08-2] (5.600 g, 26.400 mmol) in ethanol (40 mL) was added sodium borohydride (2.0 g, 53 mmol) under nitrogen at 0 °C. The reaction was stirred for 2 h. Ethanol was removed under reduced pressure. The concentrate was diluted with ethyl ether (100 mL) and washed with H₂O (2x100 mL). The organic extract was dried over Na₂SO₄, filtered, and concentrated. Silica gel chromatography (1:5 to 1:4 gradient; ethyl acetate/hexanes) of the concentrate afforded two isomers, designated A, the first eluting isomer, (2.050 g, 40%) and the more polar B (1.537 g, yield = 30%), of the title compound. Isomer B was used in the subsequent reaction.

4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-[1-[(1,1-dimethylethoxy) carbonyl]pyrrolidin-2-yl]ethyl]benzenesulfonamide

To a solution of 4-chloro-N-(2,5-dichlorophenyl) benzenesulfonamide (0.100 g, 0.298 mmol), triphenylphosphine (0.230 g, 0.890 mmol), α -methyl-[N-(*tert*-butoxy carbonyl)]-L-prolinol, (isomer B, 0.200 g, 0.890 mmol) in toluene (2 mL) was added diisopropylazodicarboxylate (0.180 g, 0.890 mmol) dropwise at 0 °C under nitrogen atmosphere. The resulting mixture was allowed to warm to 22 °C with

stirring. After 18 h the mixture was washed with sat. NaHCO_3 (4 mL), brine (4 mL) and extracted with ethyl ether (4 mL). The organic extract was dried over Na_2SO_4 and filtered. Silica gel chromatography (1:4 ethyl acetate/hexanes) of the concentrate afforded the title compound (0.095 g, yield = 60%), MS (ESI) 532.

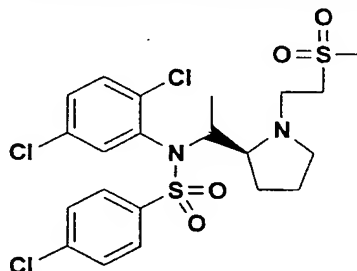
5 **4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-pyrrolidin-2-yl]ethyl]benzene sulfonamide**



To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-[1-[(1,1-dimethylethoxy)carbonyl]pyrrolidin-2-yl]ethyl]benzenesulfonamide (0.095 g, 0.178 mmol) was added a solution of 1:1 trifluoroacetic acid/ CH_2Cl_2 (2 mL) at 22 °C. The mixture was stirred for 1 h at 22 °C.

10 The solvent and trifluoroacetic acid were removed by reduced pressure to afford the title compound (0.075 g, yield = 98%), MS (ESI) 432.

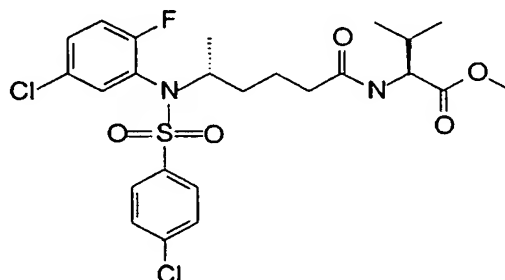
4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-[1-[2-(methylsulfonyl) ethyl]pyrrolidin-2-yl]ethyl]benzenesulfonamide



15 To a solution of 4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-pyrrolidin-2-yl]ethyl]benzenesulfonamide (0.075 g, 0.174 mmol) in THF (1 mL) was added methyl vinyl sulfone (0.060 g, 0.530 mmol) at 22 °C. The reaction was stirred for 18 h. The resulting mixture was washed with sat. K_2CO_3 (2 mL), brine (2 mL) and extracted with ethyl ether (2 mL). The organic solution was dried over Na_2SO_4 , filtered and evaporated. Silica gel chromatography (1:5 ethyl acetate/hexanes) of
20 the concentrate afforded the title compound (0.533 g, yield = 57%), MS (ESI) 538.

EXAMPLE 535

(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide

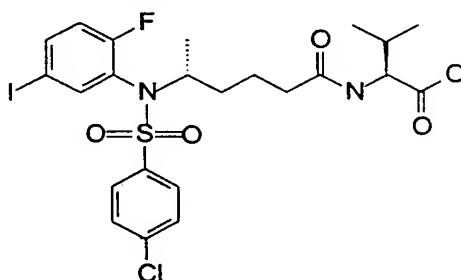


- 5 To a solution of (5R)-5-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]-hexanoyl chloride (0.265 g, 0.584 mmol) in THF (3 mL) was added Hunig's base (0.305 mL, 1.75 mmol) and L-valine methyl ester hydrochloride (0.294 g, 1.75 mmol) at 22 °C. The reaction was stirred at 22 °C temperature for 12 h. The reaction was treated with sat. NaHCO₃ (6 mL) and the aqueous phase extracted with ether (3 X 15 mL). The combined organic extracts were dried over MgSO₄,
10 filtered, and concentrated under reduced pressure. Silica gel chromatography (3:7 ethyl acetate:Hexanes) of the concentrate afforded the title compound as a light yellow wax (0.233 g, yield =73%). MS (ESI) 547 (M+H).

EXAMPLE 536

(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(carboxy)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide

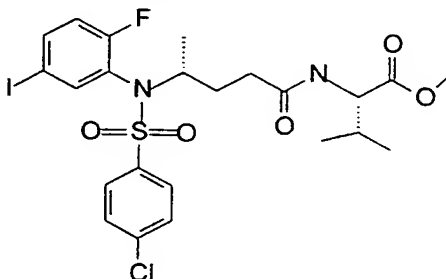
15



- To a solution of (R)-4-chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide (0.170 g, 0.310 mmol) in methanol (3.5 mL) was added NaOH (1N, 0.450 mL, 0.931 mmol) at 22 °C. The resulting mixture was heated at
20 reflux with stirring for 1.5 h. The mixture was acidified with 1N HCl and was extracted with chloroform (3 X 20 mL). The combined organic extracts were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the title compound (0.161 g, 97%) as a white powder. MS (ESI) 533 (M+H).

EXAMPLE 537

(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[N-(S)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-4-oxobutyl]benzenesulfonamide

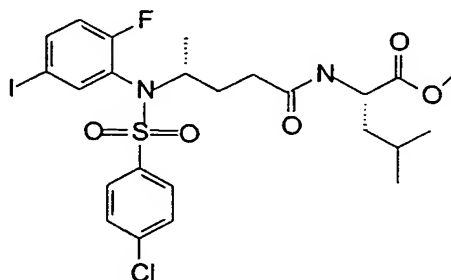


5

In a manner similar to the previous example, the title compound was prepared by reacting (4R)-4-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentanoyl chloride with L-valine methyl ester hydrochloride (71% yield). MS (ESI) 533 (M+H).

EXAMPLE 538

(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-4-oxobutyl]benzenesulfonamide



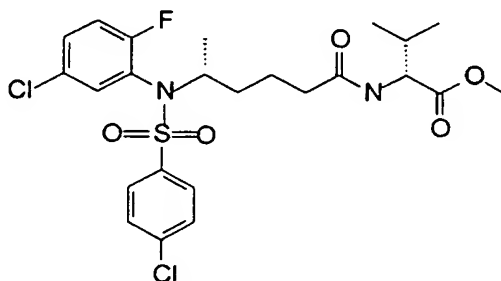
10

In a manner similar to the previous example, the title compound was prepared by reacting (4R)-4-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]pentanoyl chloride with L-leucine methyl ester hydrochloride (70% yield). MS (ESI) 547 (M+H).

15

EXAMPLE 539

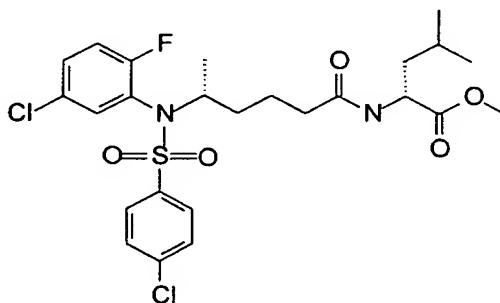
(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide



5 In a manner similar to the previous example, the title compound was prepared by reacting (5R)-5-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]hexanoyl chloride with D-valine methyl ester hydrochloride (82% yield). MS (ESI) 547 (M+H).

EXAMPLE 540

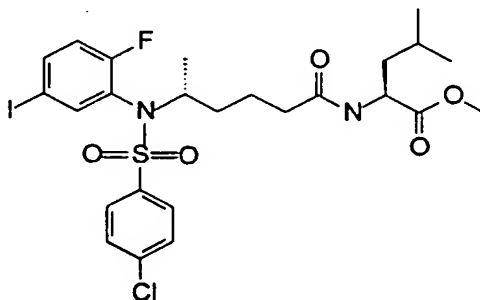
10 **(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide**



In a manner similar to the previous example, the title compound was prepared by reacting (5R)-5-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]hexanoyl chloride with D-leucine methyl ester hydrochloride (73% yield). MS (ESI) 561 (M+H).

EXAMPLE 541

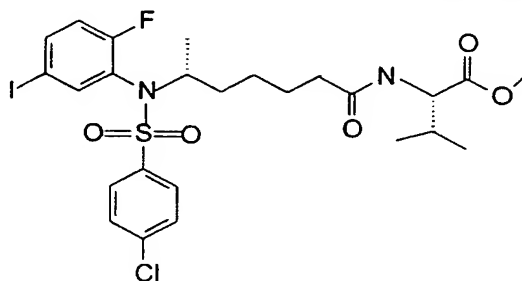
15 **(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide**



In a manner described herein, the title compound was prepared by reacting (5R)-5-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]hexanoyl chloride with L-leucine methyl ester hydrochloride to afford the title compound (71% yield). MS (ESI) 561 (M+H).

EXAMPLE 542

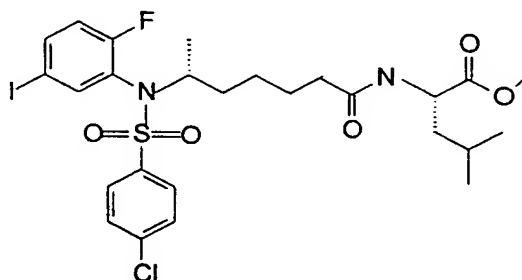
5 **(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide**



In a manner described herein, the title compound was prepared by reacting (6R)-6-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]heptanoyl chloride with L-valine methyl ester hydrochloride (85% yield). MS (ESI) 561 (M+H).

EXAMPLE 543

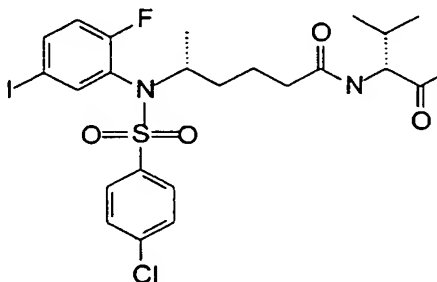
10 **(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide**



15 In a manner described herein, the title compound was prepared by reacting (6R)-6-[N-[5-chloro-2-fluorophenyl][(4-chlorophenyl)sulfonyl]amino]heptanoyl chloride with L-leucine methyl ester hydrochloride (89% yield). MS (ESI) 575 (M+H).

EXAMPLE 544

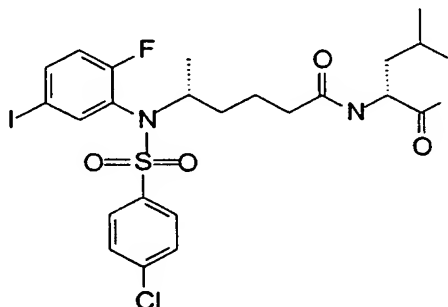
(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(carboxy)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide



5 In a manner described herein, the title compound was prepared by hydrolysis of (R)-4-chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide (90% yield). MS (ESI) 533 (M+H).

EXAMPLE 545

10 **(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(carboxy)-3-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide**

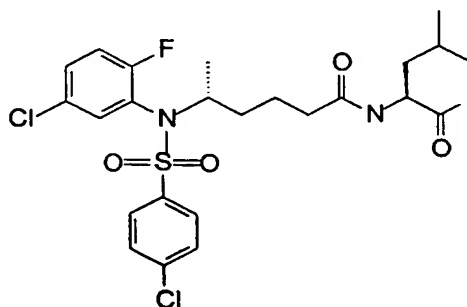


In a manner described herein, the title compound was prepared by hydrolysis of (R)-4-chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide (89% yield). MS (ESI) 547 (M+H).

15

EXAMPLE 546

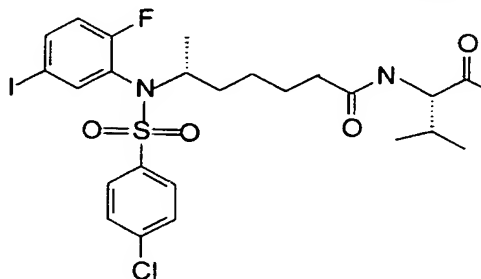
(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(carboxy)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide



In a manner described herein, the title compound was prepared by hydrolysis of (R)-4-chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide (90% yield). MS (ESI) 547 (M+H).

EXAMPLE 547

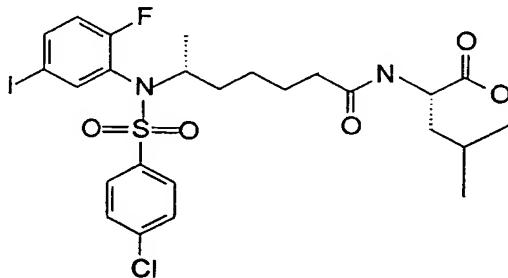
- 5 **(R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(carboxy)-2-methylpropyl]amino]-1-methyl-6-methyl-6-oxohexyl]benzenesulfonamide**



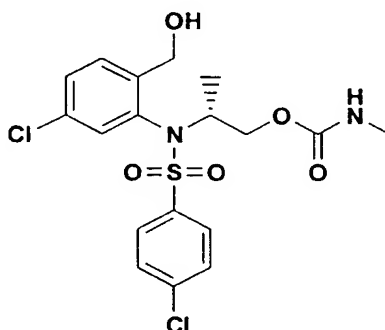
- 10 In a manner described herein, the title compound was prepared by hydrolysis of (R)-4-chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide (85% yield). MS (ESI) 547 (M+H).

EXAMPLE 548

- (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(carboxy)-3-methylbutyl]amino]-1-methyl-6-methyl-6-oxohexyl]benzenesulfonamide**



- 15 In a manner described herein, the title compound was prepared by hydrolysis of (R)-4-chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide (83% yield). MS (ESI) 561 (M+H).

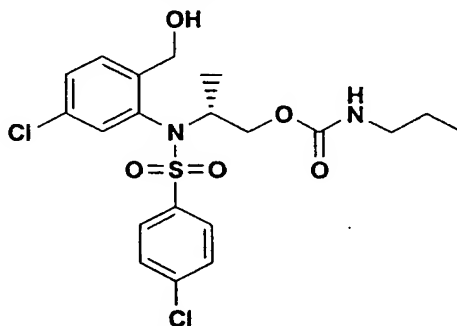
EXAMPLE 549**4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[methylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide**

5 To a solution of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[2-[[[4-nitrophenyl]oxy]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide (50mg, 0.08mmol) in DMF (2.0mL) in a 15mL HDPE cartridge was added methylamine (5.2mg,). The mixture was shaken for 12 h at 22°C in a 48 well reactor. The mixture was filtered, rinsed with ether to a test tube and concentrated by speed vacuum to afford crude 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[2-
10 [[methylamino] carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide. The molecular weight of the intermediate product was determined by LC/MS. The residue was diluted with methanol (2.0mL) in a test tube and K₂CO₃ was added. The mixture was shaken for 2 hours and filtered. The methanol was removed by speed vacuum and the residue was purified by preparative HPLC with 90% methanol/H₂O at 4mL/min. The desired product was concentrated by speed vacuum to afford the title compound.
15 Yield=32% colorless oil: LC/MS, 448(M+H); Retention Time, 3.71min.

The following carbamates were prepared as described in the previous example. They were all analyzed by LC/MS.

EXAMPLE 550

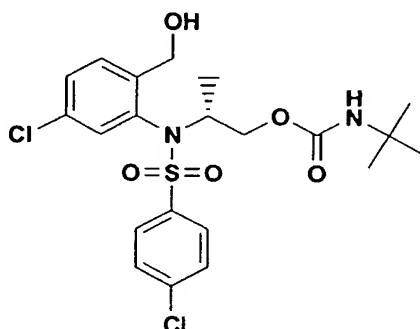
20 **4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide**



Yield=32% colorless oil: LC/MS, 476 (M+H); Retention time, 3.93min.

EXAMPLE 551

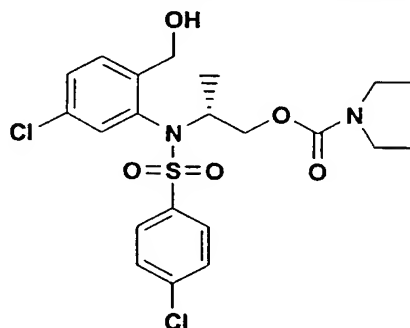
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[(1,1-dimethyl)ethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



5 Yield=35% colorless oil: LC/MS, 490 (M+H); Retention time, 4.09min.

EXAMPLE 552

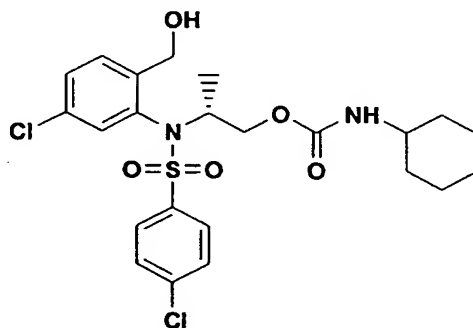
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[diethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



10 Yield=26% colorless oil: LC/MS, 490 (M+H); Retention time, 4.08min.

EXAMPLE 553

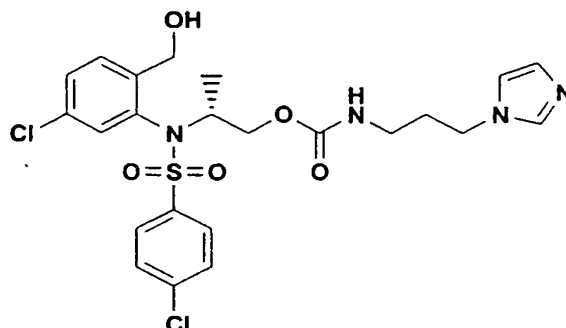
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[cyclohexylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



15 Yield=15% colorless oil: LC/MS, 516 (M+H); Retention time, 4.23min.

EXAMPLE 554

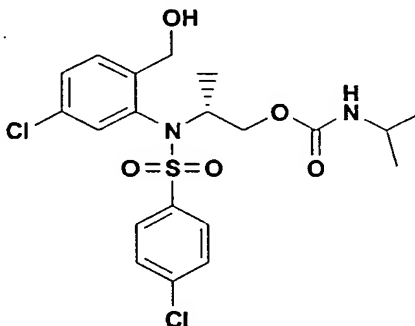
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[N'-[3-(1H-imididazol-1-yl) propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



5 Yield=30% colorless oil: LC/MS, 542 (M+H); Retention time, 4.80min.

EXAMPLE 555

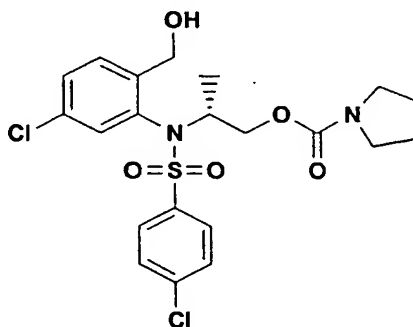
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[isopropylamino] carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



10 Yield=30% colorless oil: LC/MS, 476 (M+H); Retention time, 3.92min.

EXAMPLE 556

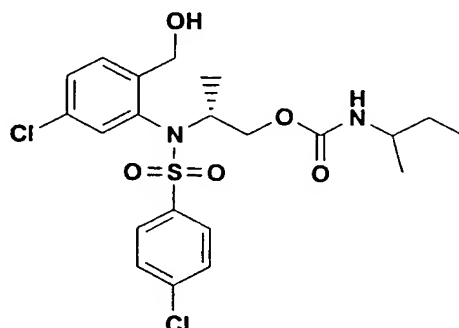
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[pyrrolidin-1-yl] carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



15 Yield=32% colorless oil: LC/MS, 488 (M+H); Retention time, 4.20min

EXAMPLE 557

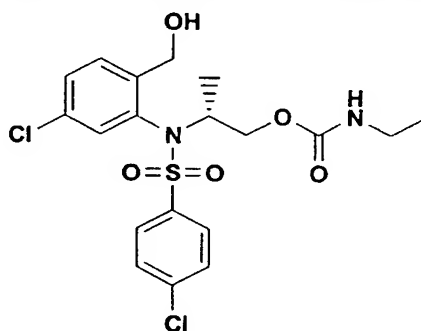
**4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[(1-methyl)propylamino] carbonyl]oxy]-
(R)-1-methylethyl]benzenesulfonamide**



5 Yield=33% colorless oil: LC/MS, 490 (M+H); Retention time, 4.05min.

EXAMPLE 558

**4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[ethylamino]carbonyl]oxy]-(R)-1-
methylethyl]benzenesulfonamide**

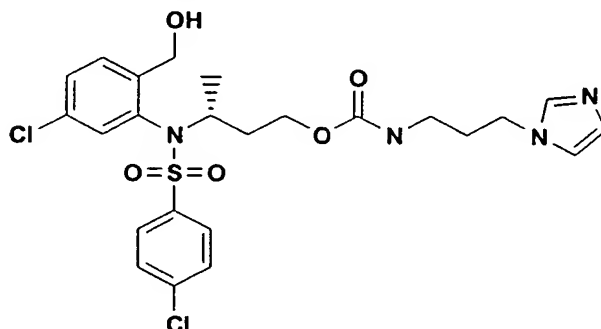


10 To a solution of 4-chloro-N-[5-chloro-2-(acetoxymethyl)phenyl]-N-[2[[[4-nitrophenyl]oxy]carbonyl]oxy]-(R)-methylethyl]benzenesulfonamide (0.85g, 0.14 mmol) was added ethylamine (0.13g, 0.28mmol) in DMF (2mL). The resulting mixture was allowed to stir at 22°C for 12 h and concentrated under reduced pressure. The mixture was diluted with methanol/ H₂O (2mL), followed by the addition of K₂CO₃. The mixture was filtered and the solvent was removed. Silica gel
15 chromatography (30% ethyl acetate/hexanes) of the concentrate afforded the title compound. Yield=90% colorless oil: MS (ESI+), 462 (M+H).

The following carbamates were prepared as described in the previous example.

EXAMPLE 559

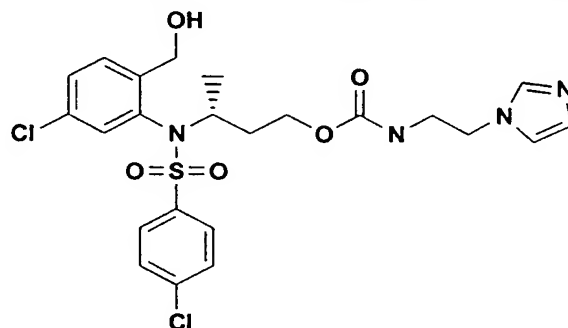
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[3-[[N'-[3-(1H-imidazol-1-yl)propylamino]carbonyl]oxy]-(R)-1-methylpropyl]benzenesulfonamide



5 Yield=70% colorless oil: MS (ESI+), 556 (M+H).

EXAMPLE 560

4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[3-[[N'-[2-(1H-imidazol-1-yl)ethylamino]carbonyl]oxy]-(R)-1-methylpropyl]benzenesulfonamide



10 Yield=75% colorless oil: MS (ESI+), 542 (M+H).

EXAMPLE 561

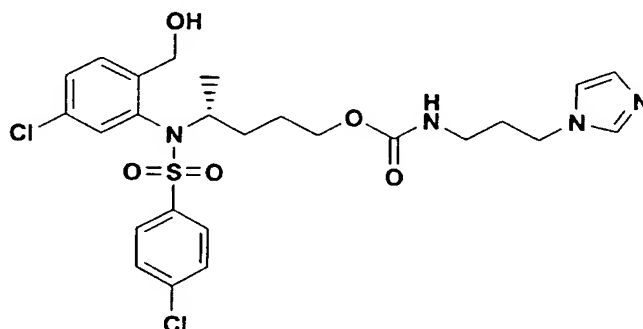
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[[N'-[2-(1H-imidazol-1-yl)ethylamino]carbonyl]oxy]-(R)-1-methylbutyl]benzenesulfonamide



15 Yield=70% colorless oil: MS (ESI+), 556 (M+H).

EXAMPLE 562

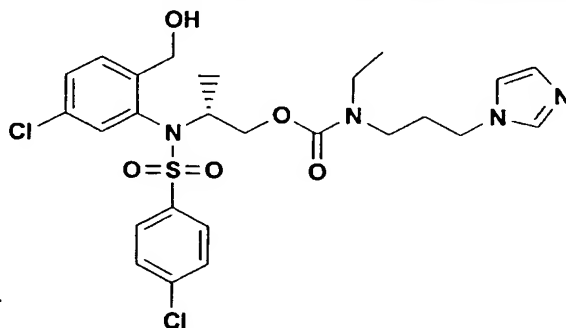
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[[N'-[3-(1H-imidazol-1-yl)propylamino]carbonyl]oxy]-(R)-1-methylbutyl]benzenesulfonamide



5 Yield=75% colorless oil: MS (ESI+), 570 (M+H).

EXAMPLE 563

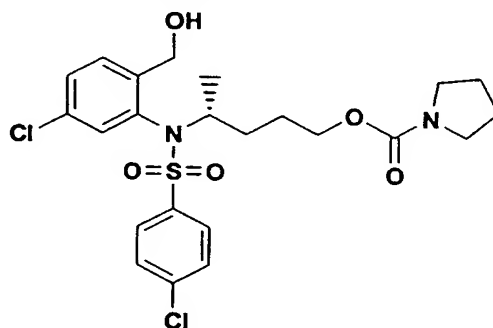
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[[N'-[3-(1H-imidazol-1-yl)propyl]-N'-ethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



10 Yield=70% colorless oil: MS (ESI-), 567 (M-H).

EXAMPLE 564

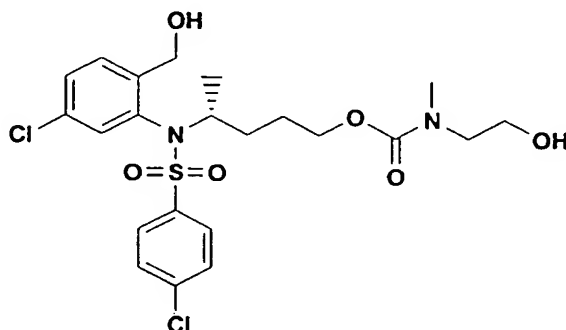
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[[pyrrolidin-1-yl]carbonyl]oxy]-(R)-1-methylbutyl]benzenesulfonamide



15 Yield=70% colorless oil: MS (ESI+), 516 (M+H).

EXAMPLE 565

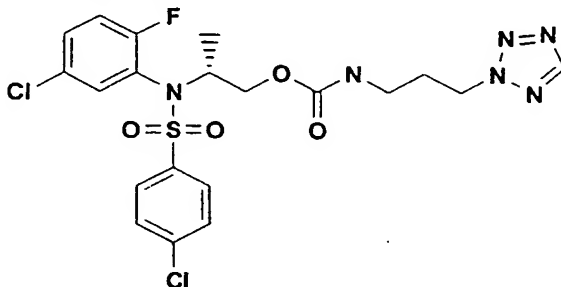
4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[[N'-[2-(hydroxyethyl)-N'-methylamino]carbonyl]oxy]-(R)-1-methylbutyl]benzenesulfonamide



5 Yield=65% colorless oil: MS (ESI+), 520 (M+H).

EXAMPLE 566

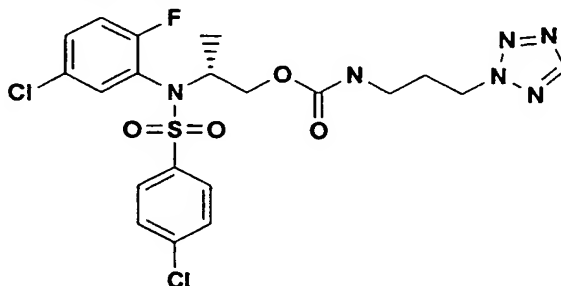
4-Chloro-N-(2-fluoro-5-chlorophenyl)-N-[2-[[N'-[3-(1H-tetrazol-1-yl)propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide



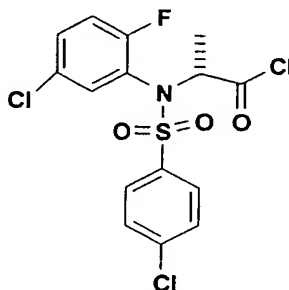
10 Yield=76% colorless oil: MS (ESI+), 532 (M+H).

EXAMPLE 567

4-Chloro-N-(2-fluoro-5-chlorophenyl)-N-[2-[[N'-[3-(1H-tetrazol-2-yl)propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide

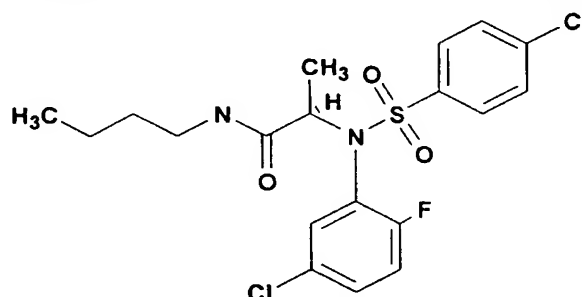


15 Yield=70% colorless oil: MS (ESI+), 532 (M+H).

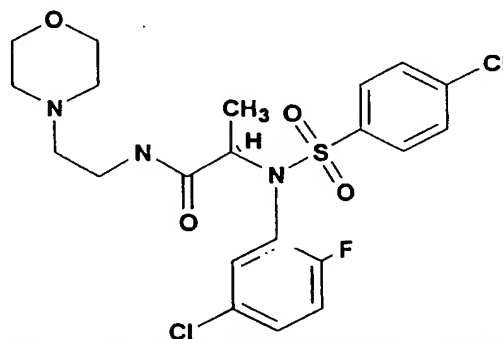
EXAMPLE 568**4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide**

5 To a stirred solution of 4-chloro-N-(5-chloro-2-fluorophenyl)sulfoanilide (10 g, 31.23 mmol), triphenylphosphine (12.5 g, 45.99 mmol), and ethyl-(s)-lactate (5.43g,, 45.99mmol) in THF (300 mL) was added diethylazodicarboxylate (11.94, 68.62 mmol) dropwise at 0 °C under nitrogen. The reaction mixture was allowed to warm to room temp and stirred for 18 h. and further diluted with ethyl acetate (1 L) and washed with water (2 x 500 mL), brine (1 x 500 mL) and dried over MgSO₄. Filtration and
10 concentration in vacuo, followed by silica gel chromatography (5% ethyl acetate / hexane) of the concentrate produced the 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(ethoxycarbonyl)]ethyl]-benzenesulfonamide compound, in 80 % yield (10.5g).

To the solution of above ester (2 g, 4.76 mmol) in THF:MeOH:H₂O/50:20:5 was added Lithium hydroxide (0.29g, 7.14mmol) and further stirred the reaction mixture for 2h. The reaction
15 mixture was diluted with 1N HCl (100 mL) and then extracted with ethyl acetate(2 x 150 mL). The organic layer was washed with brine and dried over MgSO₄, filtered, and concentrated to give 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(carboxyethyl)]benzenesulfonamide as white solid in 75 % yield (1.4g). ¹H NMR (DMSO) 7.92–7.29 (m, 7 H), 4.60–4.58 (d, 1 H), 4.04–4.01 (q, 1 H), 1.11–1.09 (d, 2 H), MS (ESI+) 391.87 (M + H)⁺. Further, the resulting carboxylic acid (1.3g , 3.31mmol) was
20 dissolved in CH₂Cl₂ (50 mL) and DMF (0.3 mL) and oxalyl chloride (0.34mL, 3.97 mmol) was added to it. The resulting reaction mixture was stirred at rt for 1 h. It was then concentrated under reduced pressure to provide the title compound in 95 % yield.

EXAMPLE 569**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(butylamino)carbonyl]ethyl]benzenesulfonamide**

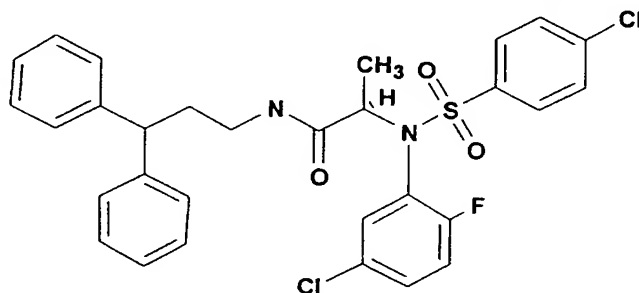
- 5 To the solution of N-butylamine (5.5 mg, 0.075 mmol) in 1,2 dichloroethane(0.75 mL) in a minireactors was added 2% cross linked poly(4-vinyl pyridine) (12.00 mg, 0.105 mmol) resin and solution(0.1 M) of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzene-sulfonamide (12.30 mg, 0.030mmol) in 1,2 dichloromethane. The mini reactor was stirred on the shaker for 12 h, followed by quenching the reaction mixture with SCX (92 mg, 0.06mmol) resin and further
- 10 stirred on the shaker for additional 18 h. Filtered off the resin and washed the resin 1,2 dichloroethane (2 x 0.2mL) and combined solvent was collected in microtube and evaporated and the product was analyzed by HPLC using the column YMC S7 C18 (3.0 x 50 mm) with a flow rate of 5.0 mL/min and gradient time of 2.0 min., using the solvent composition of 10% MeOH – 90% H₂O – 0.1% TFA , 90% MeOH –10% H₂O – 0.1% TFA. The title compound was obtained with 77% purity in 54% yield; MS
- 15 (ESI) 446.98 (M+H); R_f = 1.87.

EXAMPLE 570**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide**

- 20 In a manner described herein, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-(2-aminoethyl)morpholine (25% yield); MS (ESI) 503.99 (M+H); R_f 1.70.

EXAMPLE 571

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(3,3-diphenylpropyl)amino]carbonyl]ethyl]benzenesulfonamide

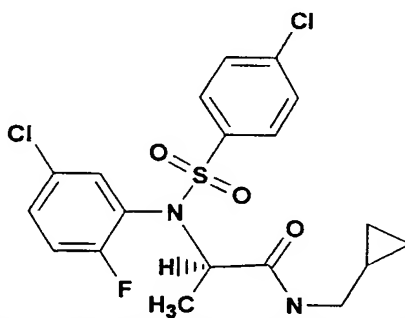


5

In a manner described herein, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 3,3-diphenylpropylamine (94% yield); MS (ESI) 584.96 (M+H); R_f 2.1.

EXAMPLE 572

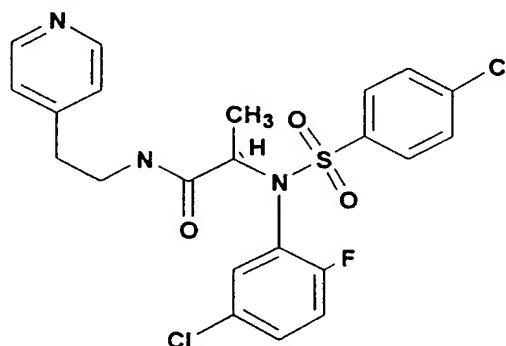
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(cyclopropylmethyl)amino]carbonyl]ethyl]benzenesulfonamide



15 In a manner described herein, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with (aminomethyl)cyclopropane (47% yield); MS (ESI) 444.95 (M+H); R_f 1.80.

EXAMPLE 573

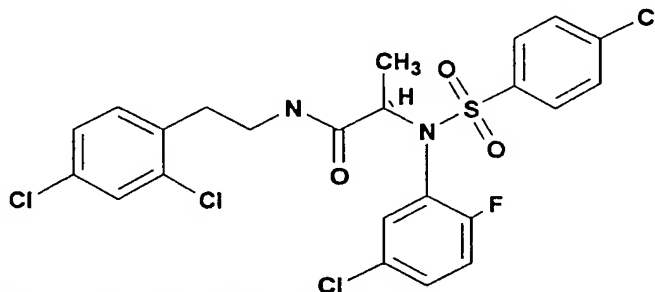
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2-(4-pyridinyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)ethyl]benzenesulfonamide with 4-(2-aminoethyl)pyridine (30% yield) MS (ESI) 495.92 (M+H); R_f 1.49.

EXAMPLE 574

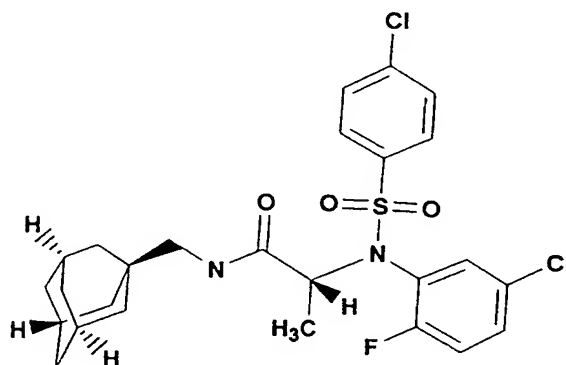
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2-(2,4-dichlorophenyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)ethyl]benzenesulfonamide with 2,4-dichlorophenethylamine. (>95% yield); MS (ESI) 562.84 (M+H); R_f 2.12.

EXAMPLE 575

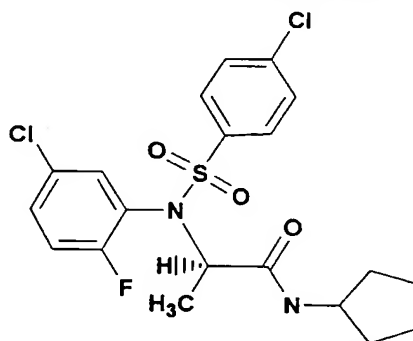
**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-
[[[adamantylmethyl]amino]carbonyl]ethyl]benzenesulfonamide**



5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 1-adamantanemethylamine (> 95% yield); MS (ESI) 538.98 (M+H); R_f 2.17.

EXAMPLE 576

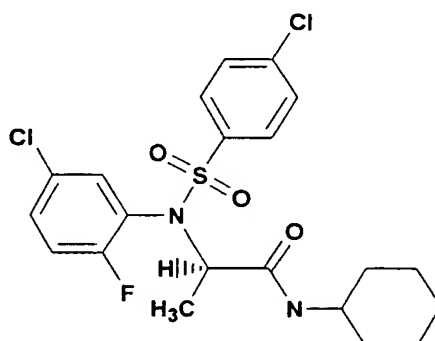
**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-
[(cyclopentylamino)carbonyl]ethyl]benzenesulfonamide**



10 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[1-(chlorocarbonyl)]ethyl]benzenesulfonamide with cyclopentylamine (61% yield) MS (ESI) 458.98 (M+H); R_f 1.88.

EXAMPLE 577

**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-
[(cyclohexylamino)carbonyl]ethyl]benzenesulfonamide**

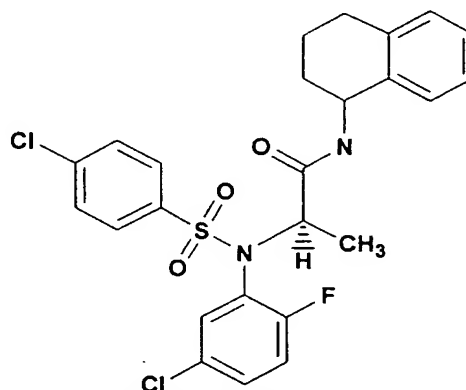


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)ethyl]benzenesulfonamide with cyclohexylamine (>95% yield); MS (ESI) 473.00 (M+H); R_f 1.95.

EXAMPLE 578

**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(1,2,3,4-tetrahydro-1-
naphthalenyl)amino]carbonyl]ethyl]benzenesulfonamide**

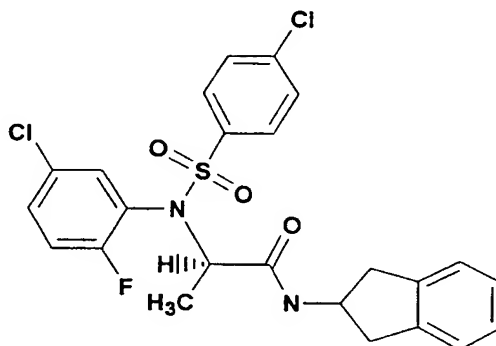
10



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)ethyl]benzenesulfonamide 1,2,3,4-tetrahydro-1-naphthylamine (> 95% yield); MS (ESI) 520.96 (M+H); R_f 2.02.

EXAMPLE 579

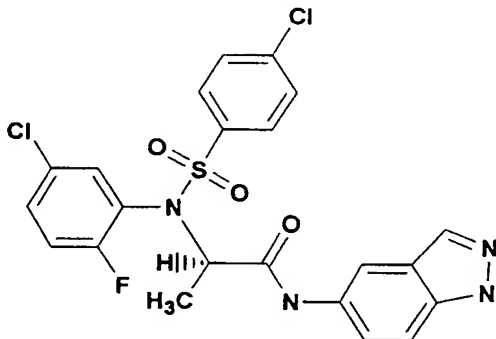
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(2,3-dihydro-1H-indenyl)amino]carbonyl]ethyl]benzenesulfonamide



5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-aminoindan (86% yield); MS (ESI) 506.96 (M+H); R_f 1.97.

EXAMPLE 580

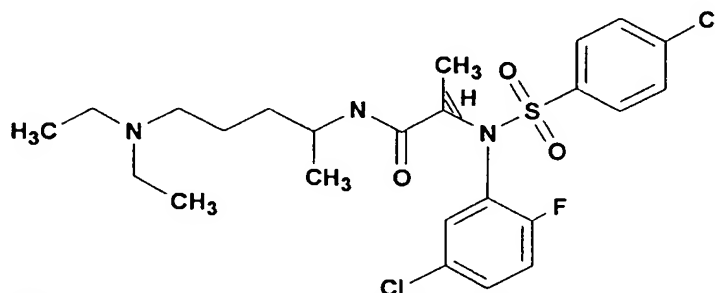
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(1H-indazol-5-yl)amino]carbonyl]ethyl]benzenesulfonamide



10 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 5-aminoindazole (97% yield); MS (ESI) 506.95 (M+H); R_f 1.74.

EXAMPLE 581

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[4-(N,N-diethylamino)-1-methylbutyl]amino]carbonyl]ethyl]benzenesulfonamide

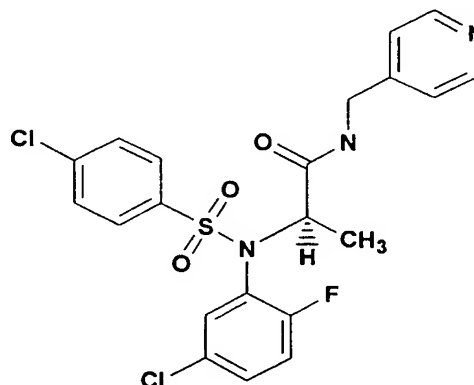


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)ethyl]benzenesulfonamide with 2-amino-5-diethylaminopentane (< 95% yield); MS (ESI) 532.03 (M+H); R_f 1.58.

EXAMPLE 582

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[4-(pyridinyl)methyl]amino]carbonyl]ethyl]benzenesulfonamide

10

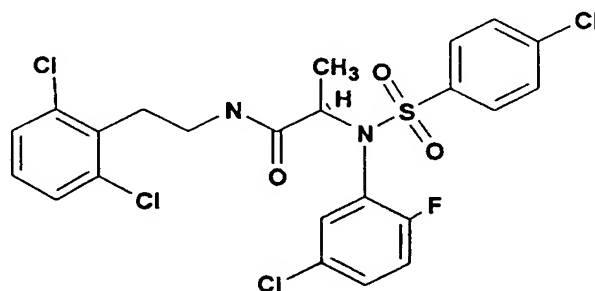


In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)ethyl]benzenesulfonamide with 4-(aminomethyl)pyridine (28 % yield); MS (ESI) 481.93 (M+H); R_f 1.69.

15

EXAMPLE 583

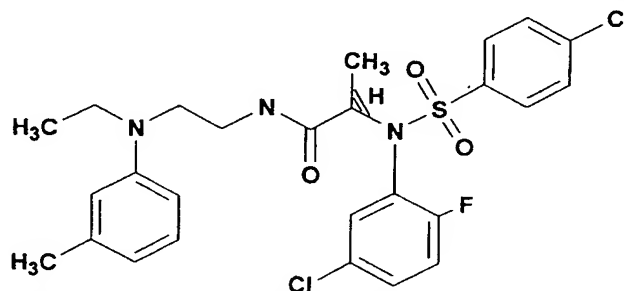
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2,6-dichlorophenyl]ethyl]amino]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2,6-dichlorophenethylamine (94% yield); MS (ESI) 562.98 (M+H); R_f 2.04.

EXAMPLE 584

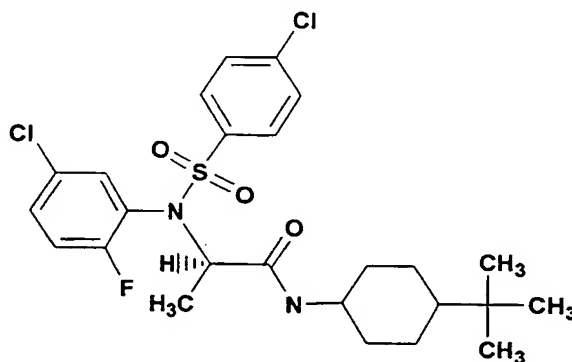
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2-[N-ethyl-N-(3-methylphenyl)amino]ethyl]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with N-(2-aminoethyl)-N-ethyl-M-toluidine (< 95% yield); MS (ESI) 551.99 (M+H); R_f 1.72.

EXAMPLE 585

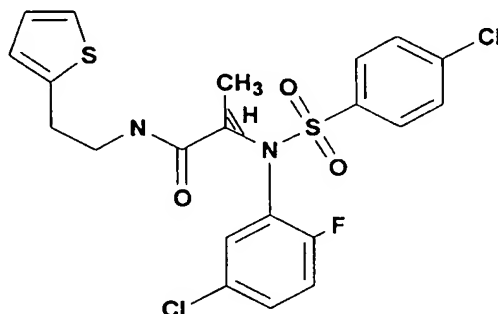
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[4-tert-butylcyclohexyl]amino]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-tert-butylcyclohexylamine (< 95% yield); MS (ESI) 529.03 (M+H); R_f 2.20.

EXAMPLE 586

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[2-(2-thienyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide

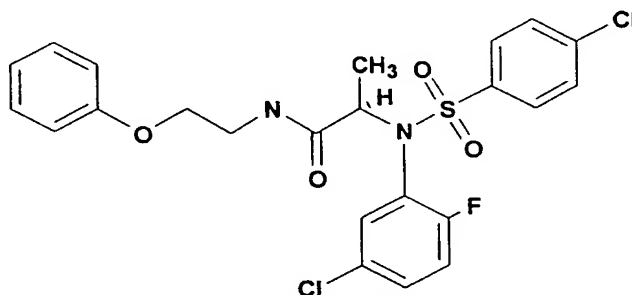


5

In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-thiopheneethylamine (>95% yield); MS (ESI) 500.91 (M+H); R_f 1.90.

EXAMPLE 587

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[2-phenoxyethyl]amino]carbonyl]ethyl]benzenesulfonamide



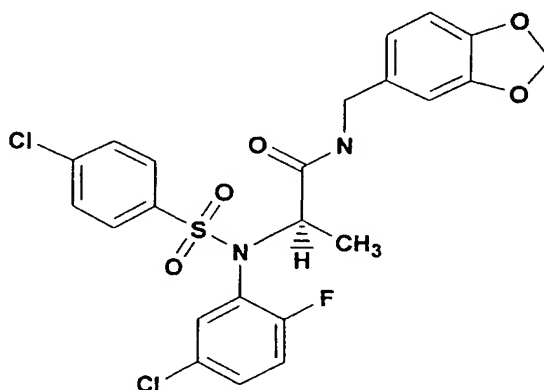
10

In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-phenoxyethylamine (>95% yield); MS (ESI) 510.95 (M+H); R_f 1.92.

15

EXAMPLE 588

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(1,3-benzodioxol-5-yl)methyl]amino]carbonyl]ethyl]benzenesulfonamide

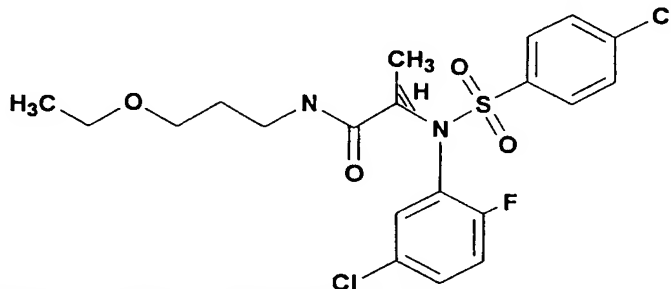


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 3,4-methylenedioxybenzylamine (>95% yield); MS (ESI) 524.93 (M+H); R_f 1.84.

EXAMPLE 589

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[3-ethoxypropyl]amino]carbonyl]ethyl]benzenesulfonamid

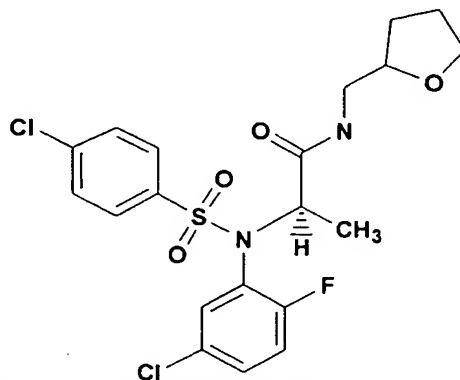
10



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 3-ethoxypropylamine (>95% yield); MS (ESI) 476.99 (M+H); R_f 1.79.

EXAMPLE 590

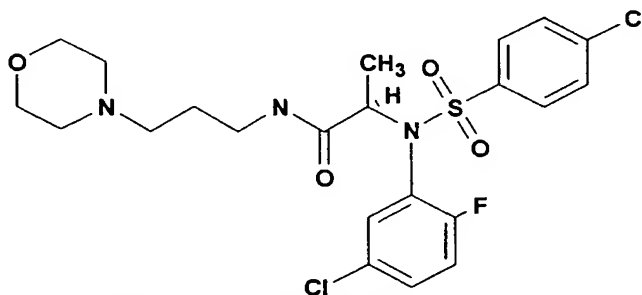
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(2-tetrahydrofuranyl)methyl]amino]carbonyl]ethyl]benzenesulfonamide



5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with tetrahydrofurfurylamine (93% yield); MS (ESI) 474.99 (M+H); R_f 1.75.

EXAMPLE 591

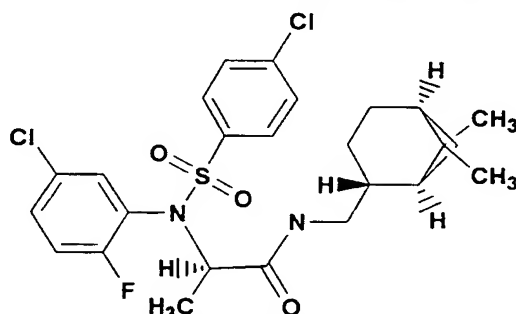
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[3-(4-morpholinyl)propyl]amino]carbonyl]ethyl]benzenesulfonamide



10 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-(3-aminopropyl)morpholine (44% yield); MS (ESI) 518.00 (M+H); R_f 1.51.

EXAMPLE 592

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(2R)-6,7-dimethylbicyclo[3.1.1]heptan-2-yl]methyl]amino]carbonyl]ethyl]benzenesulfonamide

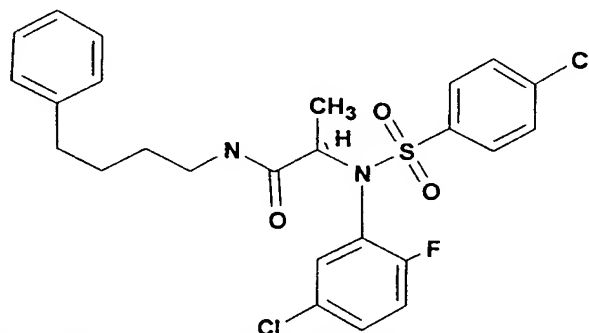


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with (-)-cis-myrtanylamine (>95% yield); MS (ESI) 527.01 (M+H); R_f 2.14.

EXAMPLE 593

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(4-phenylbutyl)amino]carbonyl]ethyl]benzenesulfonamide

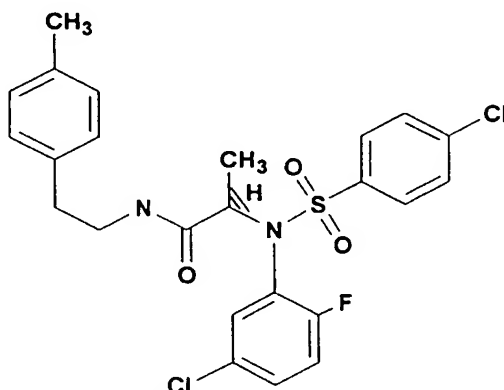
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In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-phenylbutylamine (>95% yield); MS (ESI) 522.98 (M+H); R_f 2.03.

EXAMPLE 594

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[2-(4-methylphenyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide

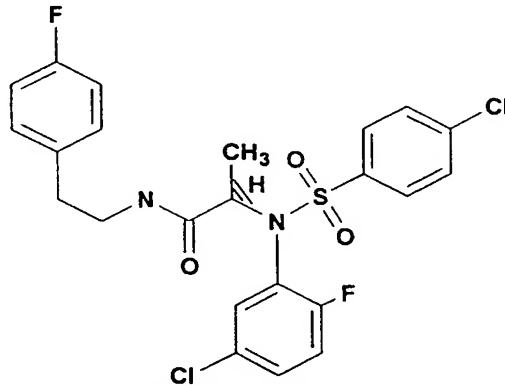


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-(p-tolyl)ethylamine (69% yield); MS (ESI) 508.95(M+H); R_f 2.01.

EXAMPLE 595

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[2-(4-fluorophenyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide

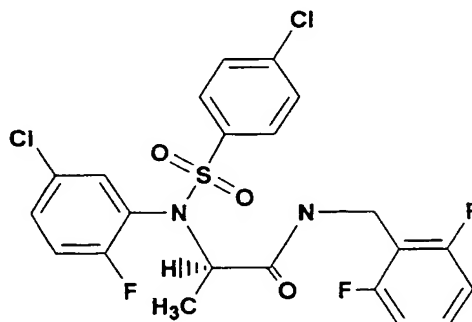
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In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-fluorophenethylamine (68% yield); MS (ESI) 512.94 (M+H); R_f 1.94.

EXAMPLE 596

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(2,6-difluorophenylmethyl)amino]carbonyl]ethyl]benzenesulfonamide

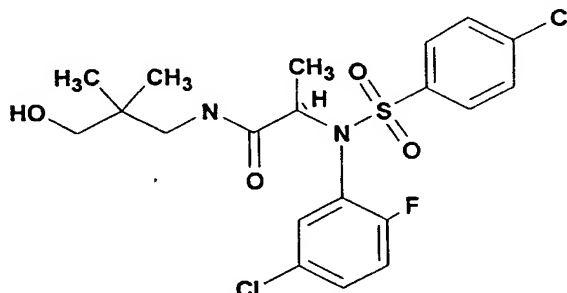


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2,6-difluorobenzylamine (75% yield); MS (ESI) 516.93 (M+H); R_f 1.86.

EXAMPLE 597

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(3-hydroxy-2,2-dimethylpropyl)amino]carbonyl]ethyl]benzenesulfonamide

10

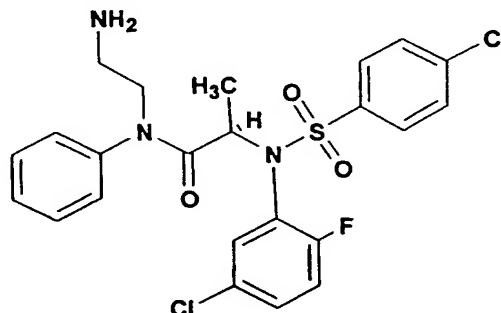


In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with neopentanolamine (73% yield); MS (ESI) 476.99 (M+H); R_f 1.74.

15

EXAMPLE 598

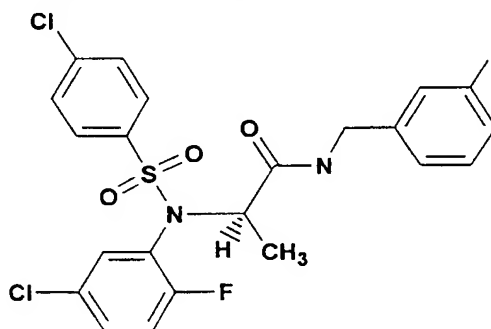
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[N-(2-aminoethyl)-N-phenylamino]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl] benzenesulfonamide with N-phenylethylenediamine (>95% yield); MS (ESI) 509.97 (M+H); R_f 1.72.

EXAMPLE 599

5 **4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(3-iodophenylmethyl) amino]carbonyl]ethyl]benzenesulfonamide**

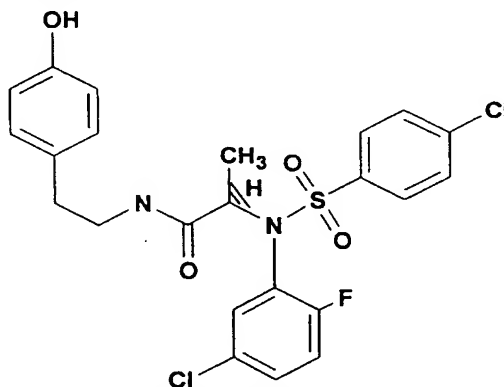


In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]

10 benzenesulfonamide with 3-iodobenzylamine (>95% yield); MS (ESI) 606.78 (M+H); R_f 2.01.

EXAMPLE 600

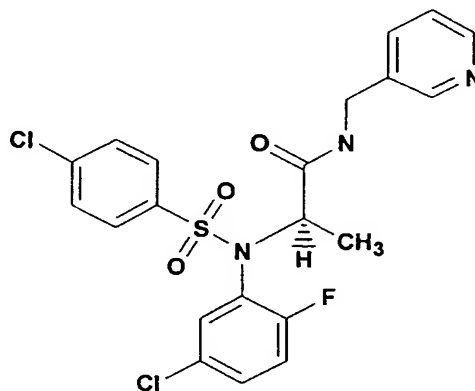
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[2-(4-hydroxyphenyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide



15 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with tyramine (44% yield); MS (ESI) 510.94 (M+H); R_f 1.73.

EXAMPLE 601

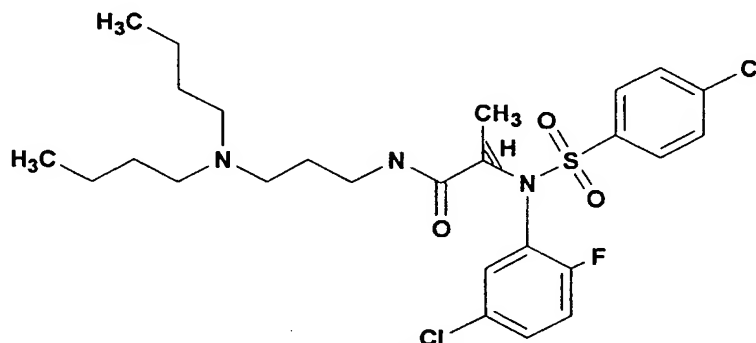
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(3-pyridinyl)methyl]amino]carbonyl]ethyl]benzenesulfonamide



5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl benzenesulfonamide with 3-(aminomethyl)pyridine (15% yield); MS (ESI) 481.95 (M+H); R_f 1.49.

EXAMPLE 602

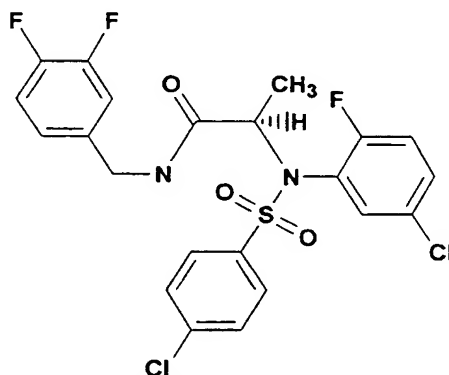
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(3-(N,N-dibutylamino)propyl]amino] carbonyl] ethyl] benzenesulfonamide



10 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl benzenesulfonamide with 3-(dibutylamino)propylamine (>95% yield); MS (ESI) 560.04 (M+H); R_f 1.74.

EXAMPLE 603

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(3,4-difluorophenyl)methyl] amino] carbonyl] ethyl]benzenesulfonamide

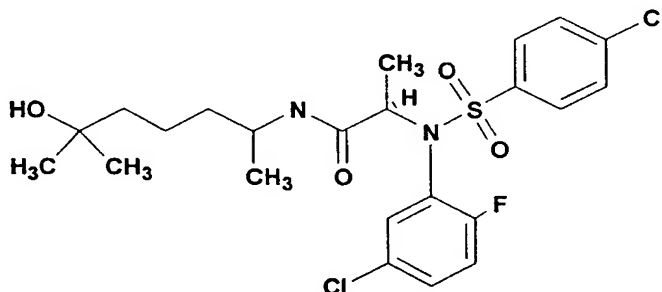


- 5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 3,4-difluorobenzylamine (>95% yield); MS (ESI) 516.93 (M+H); R_f 1.91.

EXAMPLE 604

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(5-hydroxy-1,5-dimethylhexyl) amino] carbonyl]ethyl]benzenesulfonamide

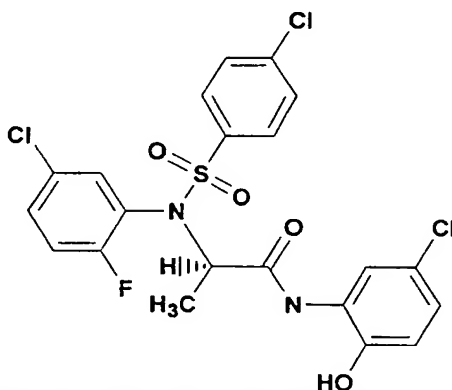
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In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl] benzenesulfonamide with heptaminol hydrochloride (22% yield); MS (ESI) 519.01 (M+H); R_f 1.69.

EXAMPLE 605

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(5-chloro-2-hydroxyphenyl)amino]carbonyl]ethyl]benzenesulfonamide

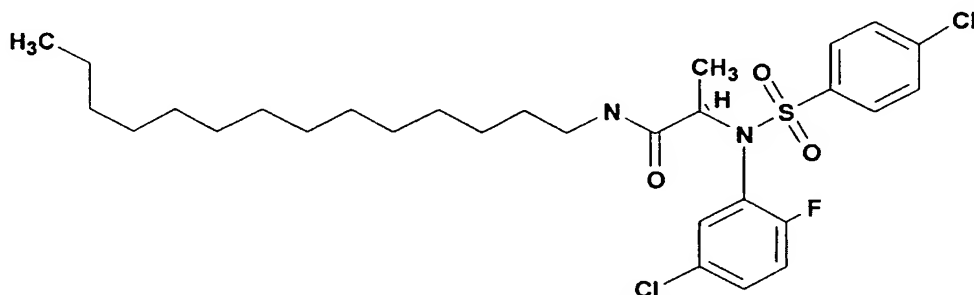


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-amino-4-chlorophenol (50% yield); MS (ESI) 516.87 (M+H); R_f 1.93.

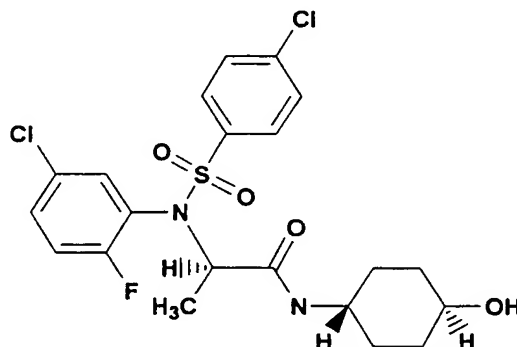
EXAMPLE 606

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(tetradecylamino)carbonyl]ethyl]benzenesulfonamide

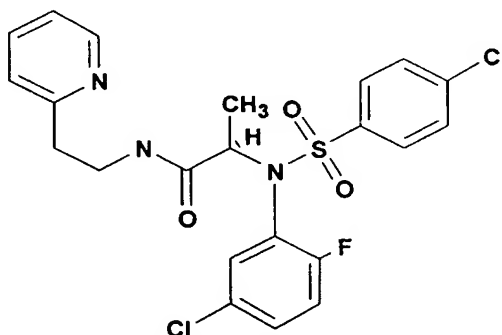
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In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 1-tetradecylamine (38% yield).; MS (ESI) 587.07 (M+H); R_f 2.73.

EXAMPLE 607**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(trans-4hydroxycyclohexyl)amino]carbonyl]ethyl]benzenesulfonamide**

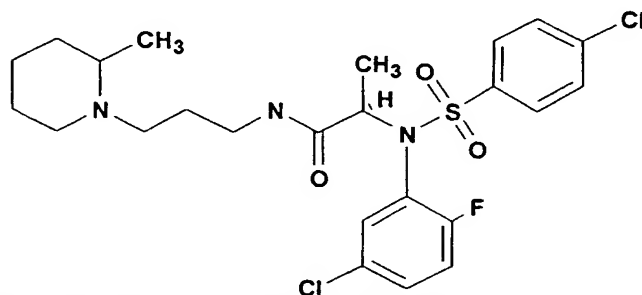
5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl] benzenesulfonamide with trans-4-aminocyclohexanol hydrochloride (29% yield); MS (ESI) 488.99 (M+H); R_f 1.69.

EXAMPLE 608**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2-(2-pyridinyl) amino]carbonyl]ethyl]benzenesulfonamide**

15 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-(2-aminoethyl)pyridine (>95% yield); MS (ESI) 495.96 (M+H); R_f 1.69.

EXAMPLE 609

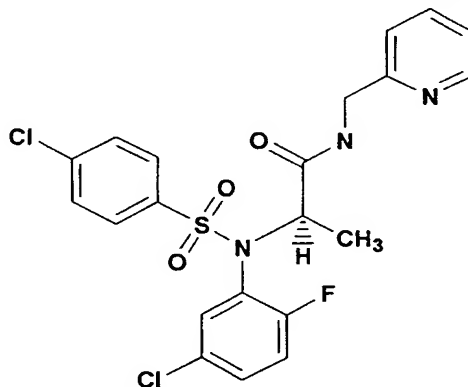
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[3-(2-methyl-1-piperidiny)]amino]carbonyl]ethyl]benzenesulfonamide



5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl] benzenesulfonamide with 1-(3-aminopropyl)-2-pipecoline (>95% yield); MS (ESI) 529.98 (M+H); R_f 1.68.

EXAMPLE 610

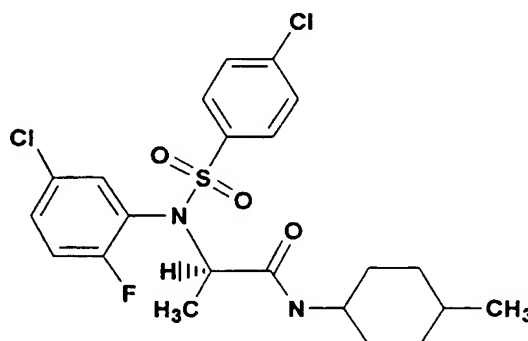
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(2-pyridinyl)methyl]amino]carbonyl]ethyl]benzenesulfonamid



10 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl] benzenesulfonamide with 2-(aminomethyl)pyridine (>95% yield); MS (ESI) 482.04(M+H); R_f 1.69.

EXAMPLE 611

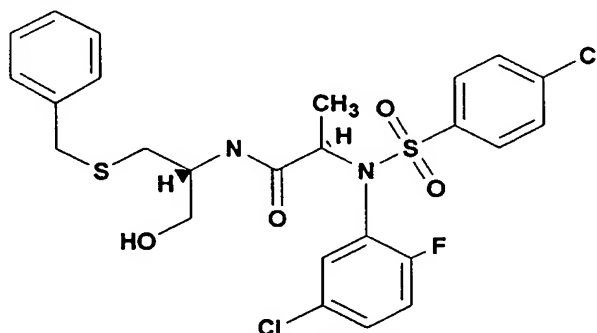
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(4-methylcyclohexyl)amino]carbonyl]ethyl]benzenesulfonamide



5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-methylcyclohexylamine (>95% yield); MS (ESI) 487.00 (M+H); R_f 2.01.

EXAMPLE 612

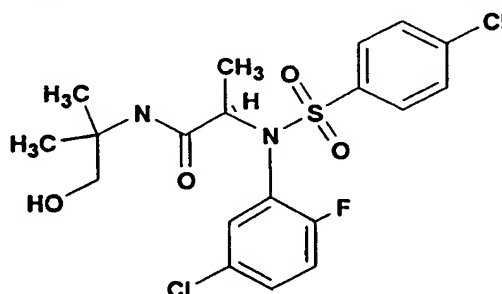
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-1-[[[(1R)-1-(hydroxymethyl)-2-[(phenylmethyl)thio]ethyl]amino]carbonyl]benzenesulfonamide



10 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with S-benzyl-L-cysteinol (75% yield); MS (ESI) 570.93 (M+H); R_f 1.95.

EXAMPLE 613

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(2-hydroxy-1,1-dimethylethyl)amino]carbonyl]ethyl]benzenesulfonamide

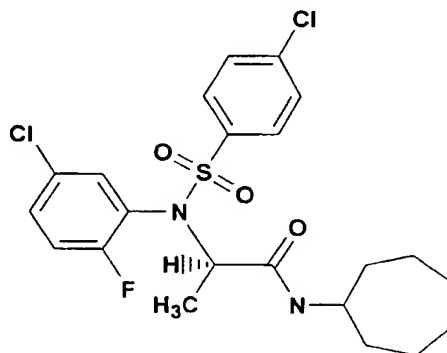


In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-amino-2-methyl-1-propanol (58% yield); MS (ESI) 462.96 (M+H); R_f 1.71.

5

EXAMPLE 614

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(cycloheptylamino)]carbonyl]ethyl]benzenesulfonamide

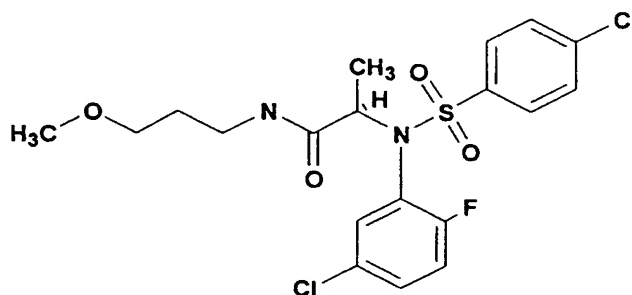


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In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with cycloheptylamine (83% yield); MS (ESI) 487.00 (M+H); R_f 2.00.

EXAMPLE 615

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(4-oxapentyl)amino]carbonyl]ethyl]benzenesulfonamide

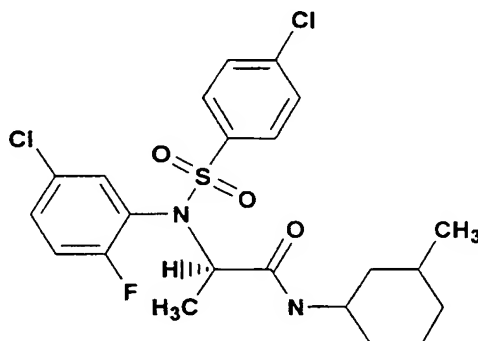


15

In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 3-methoxypropylamine (96% yield); MS (ESI) 462.97 (M+H); R_f 1.73.

EXAMPLE 616

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(3-methylcyclohexyl)amino]carbonyl]ethyl]benzenesulfonamide

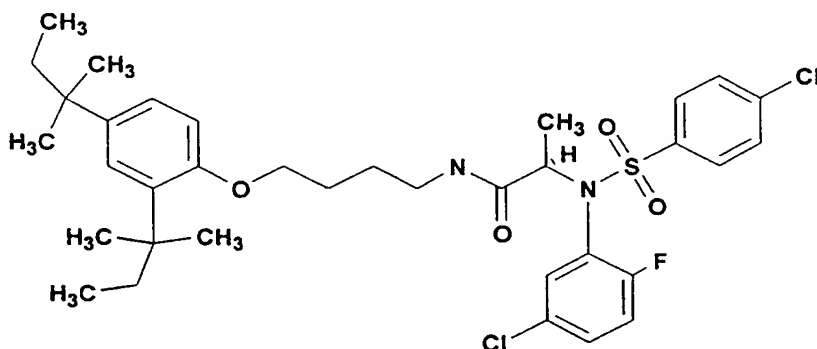


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 3-methylcyclohexylamine (76% yield); MS (ESI) 487.01 (M+H); R_f 2.01.

EXAMPLE 617

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[4-[2,4-bis(1,1-dimethylpropyl)phenoxy]butyl]amino]carbonyl]ethyl]benzenesulfonamide

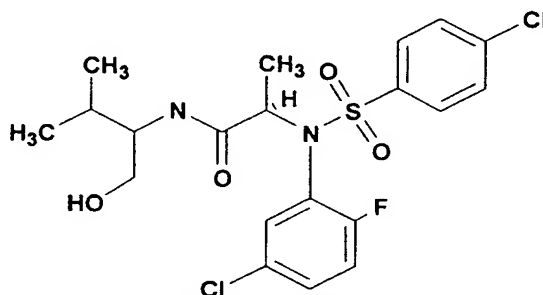
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15 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-(2,4-di-tert-amylphenoxy)butylamine (94% yield); MS (ESI) 679.1 (M+H); R_f 2.60.

EXAMPLE 618

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[1-(hydroxymethyl)-2-methylpropyl]amino]carbonyl]ethyl]benzenesulfonamide

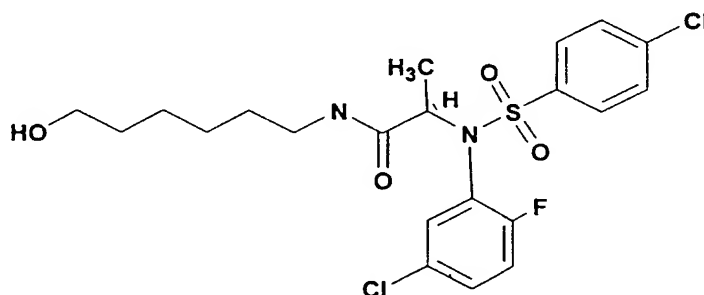


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with DL-valinol (66% yield); MS (ESI) 477.00 (M+H); R_f 1.77.

EXAMPLE 619

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(6-hydroxyhexyl)amino]carbonyl]ethyl]benzenesulfonamide

10

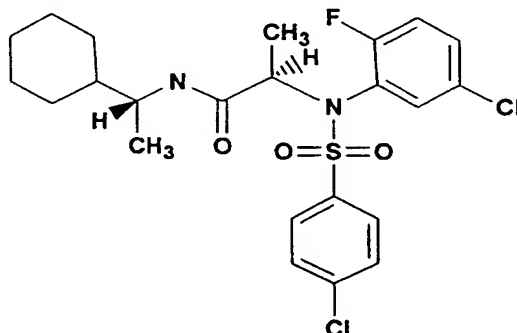


In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 6-amino-1-hexanol (39% yield); MS (ESI) 490.98 (M+H); R_f 1.72.

15

EXAMPLE 620

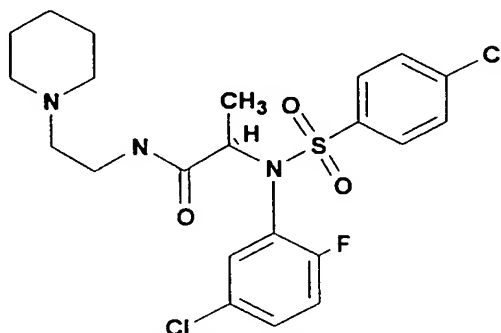
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(1R)-1-(1-cyclohexylethyl)amino]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with (R)-(-)-1-cyclohexylethylamine (76% yield); MS (ESI) 501.00 (M+H); R_f 2.07.

EXAMPLE 621

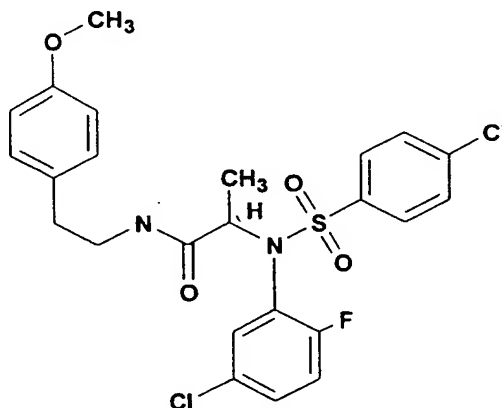
5 4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2-(piperidinyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide



10 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 1-(2-aminoethyl)piperidine (20% yield); MS (ESI) 502.05 (M+H); R_f 1.69.

EXAMPLE 622

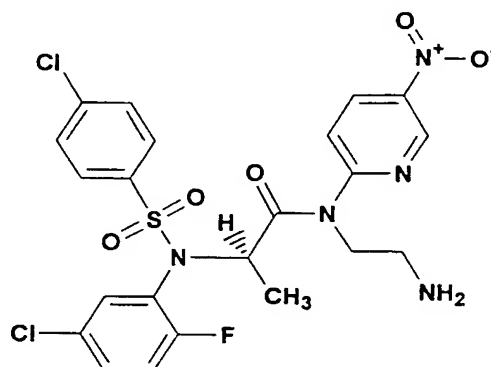
 4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2-(4-methoxyphenyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide



15 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[[[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-methoxyphenethylamine (64% yield); MS (ESI) 524.97 (M+H); R_f 1.91.

EXAMPLE 623

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[N-(2-aminoethyl)-N-(5-nitro-2-pyridinyl)amino]carbonyl]ethyl]benzenesulfonamide

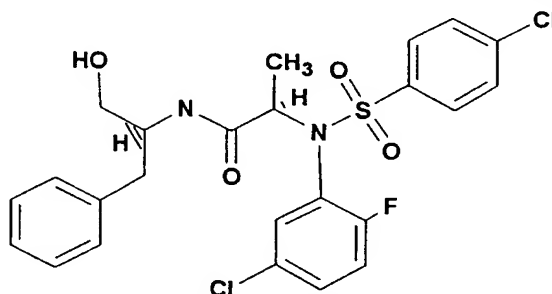


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-(2-aminoethylamino)-5-nitropyridine (>95% yield); MS (ESI) 555.93 (M+H); R_f 1.80.

EXAMPLE 624

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(1S)-2hydroxy-1-(phenylmethyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide

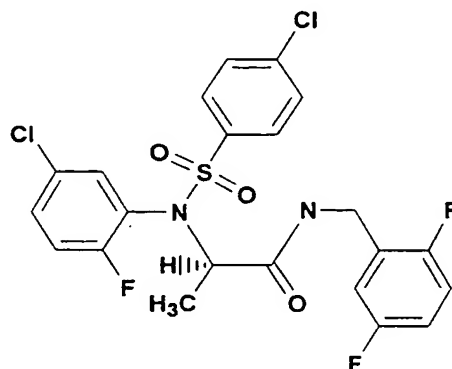
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In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with L-phenylalaninol (75% yield); MS (ESI) 524.96(M+H); R_f 1.87.

EXAMPLE 625

**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(2,5-difluorophenylmethyl) amino]carbonyl
[ethyl]benzenesulfonamide**

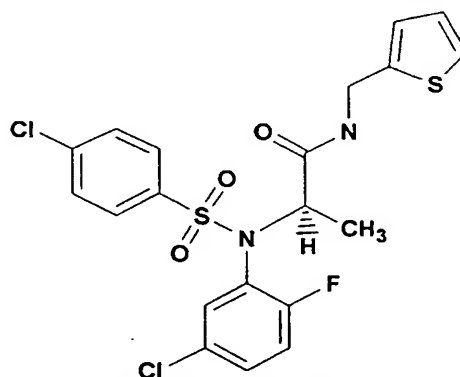


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2,5-difluorobenzylamine (93% yield); MS (ESI) 516.93 (M+H); R_f 1.88.

EXAMPLE 626

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(2-thienyl)methyl]amino]carbonyl]ethyl]benzenesulfonamide

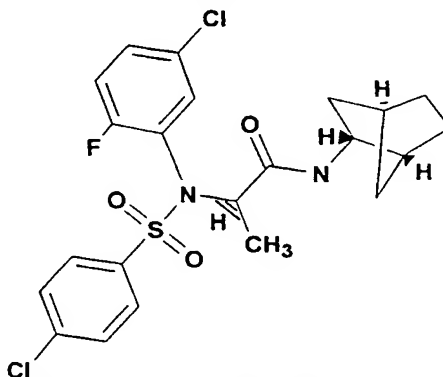
10



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-aminomethylthiophene (67% yield); MS (ESI) 486.91 (M+H); R_f 1.84.

EXAMPLE 627

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(2R)-(bicyclo[2.2.1]hept-2-yl)amino]carbonyl]ethyl]benzenesulfonamide

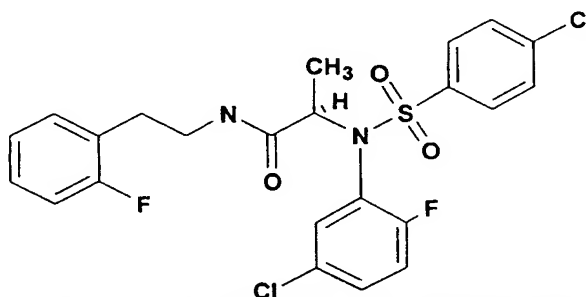


5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with exo-2-aminononobornane (77% yield); MS (ESI) 485.00 (M+H); R_f 1.96.

EXAMPLE 628

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[(2-fluorophenyl)ethyl]amino]carbonyl]ethyl]benzenesulfonamide

10

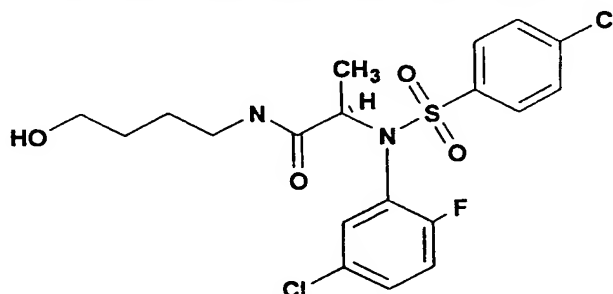


In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-fluorophenethylamine (80% yield); MS (ESI) 512.94 (M+H); R_f 1.93.

15

EXAMPLE 629

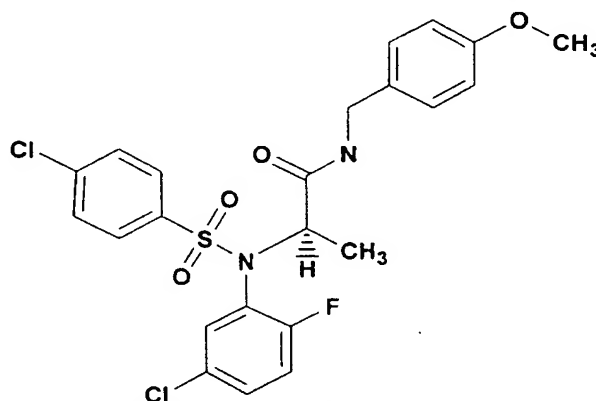
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(4-hydroxybutyl)amino]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-amino-1-butanol (24% yield); MS (ESI) 462.97 (M+H); R_f 1.63.

EXAMPLE 630

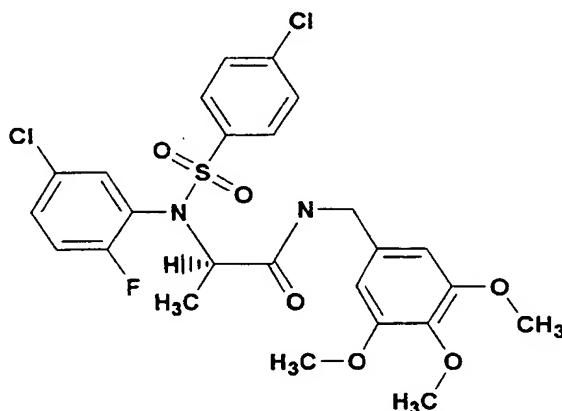
5 **4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(4-methoxyphenylmethyl)amino]carbonyl]ethyl]benzenesulfonamide**



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 4-methoxybenzylamine (60% yield); MS (ESI) 510.95 M+H); R_f 1.86.

EXAMPLE 631

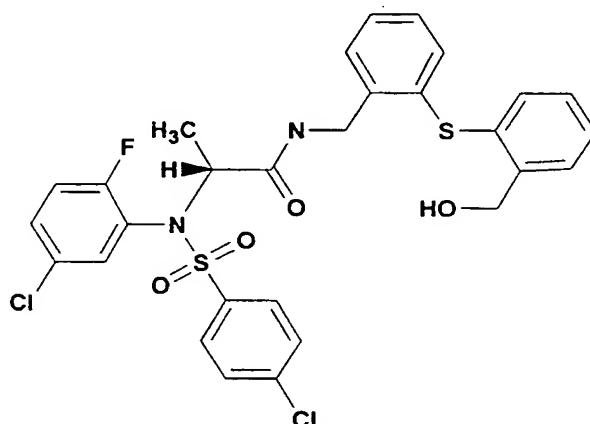
10 **4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(3,4,5-trimethoxyphenylmethyl)amino]carbonyl]ethyl]benzenesulfonamide**



15 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 3,4,5-trimethoxybenzylamine (94% yield); MS (ESI) 570.95 M+H); R_f 1.80.

EXAMPLE 632

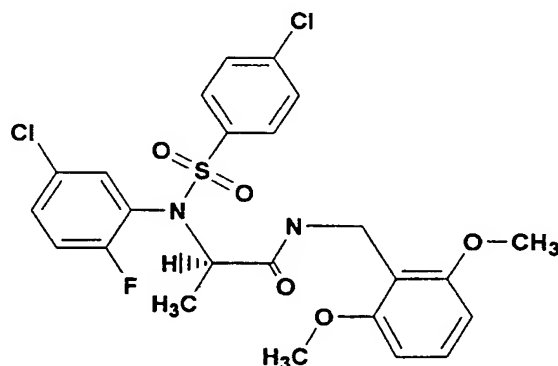
4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2-[[2-(hydroxymethyl)phenyl]thio]phenylmethyl]amino]carbonyl]ethyl]benzenesulfonamide



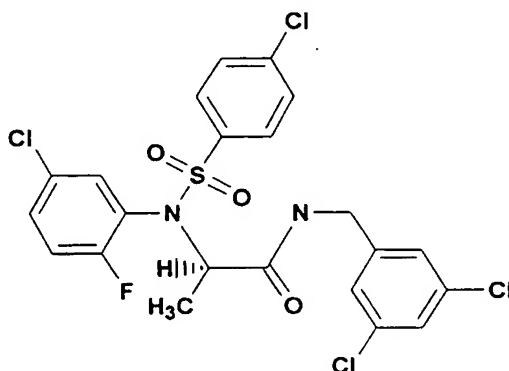
In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2-(2-(aminomethyl)phenylthio)benzylalcohol (>95% yield); MS (ESI) 618.95 (M+H); R_f 1.97.

EXAMPLE 633

4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[[2,6-dimethoxyphenylmethyl]amino]carbonyl]ethyl]benzenesulfonamide



In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 2,6-dimethoxybenzylamine (>95% yield); MS (ESI) 540.96 (M+H); R_f 1.95.

EXAMPLE 634**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[(3,5-dichlorophenylmethyl)amino]carbonyl]ethyl]benzenesulfonamide**

5 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with 3,5-dichlorobenzylamine (65% yield); MS (ESI) 548.81 (M+H); R_f 2.07.

EXAMPLE 635**4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-[[4-(1,2,3-thiadiazol-4-yl)phenylmethyl]amino]carbonyl]ethyl]benzenesulfonamide**

10 In a manner similar to previous examples, the title compound was prepared by the reaction of 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(chlorocarbonyl)]ethyl]benzenesulfonamide with R4-(1,2,3-thiadiazol-4-yl)benzylamine (84% yield); MS (ESI) 564.91 (M+H); R_f 1.82.

EXAMPLE 636**In Vitro Cell-Based Assay of Inhibitors of Amyloid β Production**

15 Transfected H4 (human neuroglioma) cells stably expressing APP constructs are used to identify and assess inhibitors of A β production. In brief, cells lines are exposed to compounds, and the effect of each compound on amyloid β production is determined by measuring the amount of amyloid β produced using an enzyme linked immunosorbent assay (ELISA) that detects amyloid β (see, for example, Seubert *et al.*, (1992) *Nature*, 359:325-327).

25 Transfected cells that stably express wild-type and variant forms of APP are plated in 96-well format plates at a density sufficient for the rapid detection of the secreted amyloid β (experimentally predetermined for a particular stable cell population). Cells are plated at least six hours prior to the introduction of the test compound at which time the growth medium is replaced by fresh medium containing the compound to be tested. All synthetic agents are initially screened at doses ranging from 10-100 μ M. Higher dilutions of agents can be used to minimize cytotoxicity. Incubation of cells with a

test compound continues for approximately 16 hours at which time aliquots of medium from each well are removed and assayed for amyloid β .

ELISA is carried out by methods known in the art (see, e.g., Haass *et al.*, *Antibodies: A Laboratory Manual*, Harlow and Lane, Editors, Cold Spring Harbor Press, 1988) The capture antibody is typically a mouse monoclonal (IgG1/k β -APPa) which recognizes the carboxyl terminal epitope of amyloid β . The specificity of the capture antibody insures measurement of amyloid β without interference from other secreted APP fragments that share amino acid sequence (amyloid β 1-16) homology with amyloid β but lack the carboxy-terminal region. The detecting antibody is typically an affinity-purified rabbit polyclonal antibody that is specific for the amino terminus of amyloid β .

Results from test compounds are compared to results obtained when cells are treated with control agents. Amyloid β levels are determined by comparison to a standard curve obtained by subjecting a range of known amounts of amyloid β to the ELISA.

A compound is identified as "active" when it inhibits cellular production of amyloid β relative to levels in control samples by at least 50% at the initial tested concentration without significant cytotoxicity. Active compounds are then assayed in dose-response experiments to determine the lowest dose of compound necessary for inhibition of amyloid β production. The results obtained when invention compounds are subjected to the above described assay results are summarized in Table B. In the table, an inhibitory concentration (IC_{50}) of less than or equal to 25 nM is represented by +++++; $50\text{nM} \geq IC_{50} > 25\text{ nM}$, by ++++; $100\text{ nM} \geq IC_{50} > 50\text{ nM}$, by +++; $500\text{ nM} \geq IC_{50} > 100\text{ nM}$, by ++; $IC_{50} > 500\text{ nM}$ is represented by +. Compounds which did not display measurable activity in this assay are represented by -.

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 1 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[4-(1,1-dioxido-4-thiomorpholinyl)-4-oxobutyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 2 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[4-(1,1-dioxido-4-thiomorpholinyl)-4-oxobutyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 3 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-oxo-4-(4-thiomorpholinyl)butyl]phenyl}ethyl)benzenesulfonamide |
| 4 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(4-methyl-1-piperazinyl)-3-oxopropyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 5 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-oxo-3-(4-thiomorpholinyl)propyl]phenyl}ethyl)benzenesulfonamide |
| 6 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1-piperidinyl)propyl]phenyl}ethyl)benzenesulfonamide |
| 7 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 8 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-[3-(1-piperidinyl)propoxy]benzyl)benzenesulfonamide hydrochloride |
| 9 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-[3-(1-piperidinyl)propoxy]benzyl)benzenesulfonamide hydrochloride |
| 10 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-[3-(1-piperidinyl)propoxy]benzyl)benzenesulfonamide hydrochloride |
| 11 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-[3-(1-piperidinyl)propoxy]benzyl)benzenesulfonamide hydrochloride |
| 12 | +++++ | methyl (2R)-2-[(tert-butoxycarbonyl)amino]-3-[[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl]sulfonyl]propanoate |
| 13 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1-piperidinyl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 14 | +++++ | ethyl 4-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]butanoate |
| 15 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(4-methyl-1-piperazinyl)-3-oxopropyl]phenyl}ethyl)benzenesulfonamide |
| 16 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(2H-tetrazol-2-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 17 | +++++ | 4-[2-((1R)-1-{5-chloro[4-(4-chlorophenyl)sulfonyl]-2-fluoroanilino]ethyl)-5-fluorophenyl]butanoic acid |
| 18 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[2-(3-pyridinylmethoxy)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 19 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[(methylamino)sulfonyl]butyl}phenyl)ethyl]benzenesulfonamide |
| 20 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[(methylamino)sulfonyl]butyl}phenyl)ethyl]benzenesulfonamide |
| 21 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(methylsulfonyl)propyl]phenyl}ethyl)benzenesulfonamide |
| 22 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[(methylamino)sulfonyl]butyl}phenyl)ethyl]benzenesulfonamide |
| 23 | +++++ | 4-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]butanoic acid |
| 24 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1-piperidinyl)butyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 25 | +++++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)benzyl 4-thiomorpholinecarboxylate |
| 26 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(ethylsulfonyl)propyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 27 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(ethylsulfonyl)propyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 28 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(4-methyl-1-piperazinyl)-4-oxobutyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 29 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[2-(4-pyridinylmethoxy)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 30 | +++++ | 5-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]pentanoic acid |
| 31 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 32 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1H-1,2,4-triazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 33 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(1H-imidazol-1-yl)butyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 34 | +++++ | 4-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]butanoic acid |
| 35 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{3-[(methylamino)sulfonyl]propyl}phenyl)ethyl]benzenesulfonamide |
| 36 | +++++ | methyl (2R)-2-[(tert-butoxycarbonyl)amino]-3-{[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl]sulfanyl}propanoate |
| 37 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-oxo-4-(1-piperidinyl)butyl]phenyl}ethyl)benzenesulfonamide |
| 38 | +++++ | 3-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]propanoic acid |
| 39 | +++++ | 3-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]propanoic acid |
| 40 | +++++ | N-(tert-butoxy)-4-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]butanamide |
| 41 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 42 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 43 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 44 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 45 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(methylsulfonyl)butyl]phenyl}ethyl)benzenesulfonamide |
| 46 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(methylsulfonyl)butyl]phenyl}ethyl)benzenesulfonamide |
| 47 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{3-[(dimethylamino)sulfonyl]propyl}-4-fluorophenyl)ethyl]benzenesulfonamide |
| 48 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(1-piperidinyl)butyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 49 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(4H-1,2,4-triazol-4-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 50 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{3-[(ethylamino)sulfonyl]propyl}-4-fluorophenyl)ethyl]benzenesulfonamide |
| 51 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1H-tetrazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 52 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[(ethylsulfonyl)methyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 53 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 54 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 55 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 56 | +++++ | 4-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]-N-methoxybutanamide |
| 57 | +++++ | N-{3-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N,2,2-trimethylpropanamide |
| 58 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-(3-hydroxybutyl)phenyl}ethyl)benzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 59 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(2-{4-[(ethylamino)sulfonyl]butyl}-4-fluorophenyl)ethyl)benzenesulfonamide |
| 60 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{4-fluoro-2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 61 | +++++ | N-{4-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-2-methoxy-N-methylacetamide |
| 62 | +++++ | methyl 3-[[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl]sulfonyl]propanoate |
| 63 | +++++ | 2-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 4-thiomorpholinecarboxylate |
| 64 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(ethylsulfonyl)propyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 65 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[4-(ethylsulfonyl)butyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 66 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[4-(ethylsulfonyl)butyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 67 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 68 | +++++ | 4-[2-(1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]butanoic acid |
| 69 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[4-fluoro-2-(4-hydroxypentyl)phenyl]ethyl)benzenesulfonamide |
| 70 | +++++ | methyl (2R)-2-[(tert-butoxycarbonyl)amino]-3-({3-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]propyl}sulfonyl)propanoate |
| 71 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-tetrazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 72 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrobromide |
| 73 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-oxo-3-(1-piperidinyl)propyl]phenyl}ethyl)benzenesulfonamide |
| 74 | +++++ | 4-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]-N-methoxy-N-methylbutanamide |
| 75 | +++++ | methyl (2R)-2-[(tert-butoxycarbonyl)amino]-3-({3-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]propyl}sulfonyl)propanoate |
| 76 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-{2-[3-(1-oxido-1-piperidinyl)propoxy]benzyl}benzenesulfonamide |
| 77 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-{2-[3-(1-oxido-1-piperidinyl)propoxy]benzyl}benzenesulfonamide |
| 78 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-oxido-1-piperidinyl)propoxy]benzyl}benzenesulfonamide |
| 79 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1,1,4-trioxido-4-thiomorpholinyl)propoxy]benzyl}benzenesulfonamide |
| 80 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1-piperidinyl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 81 | +++++ | methyl ({2-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl}sulfonyl)acetate |
| 82 | +++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 83 | +++++ | methyl 3-({2-[2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl}sulfonyl)propanoate |
| 84 | +++++ | 4-bromo-N-(2,5-difluorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 85 | +++++ | 4-chloro-N-{2-[3-(diethylnitroxy)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |
| 86 | +++++ | 4-chloro-N-{2-[3-(diethylnitroxy)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |
| 87 | +++++ | 2-((1R)-1-[[4-(chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 4-methyl-1-piperazinecarboxylate |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 88 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(2H-tetraazol-2-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 89 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-({1-[3-(1-piperidinyl)propoxy]-2-naphthyl)methyl}benzenesulfonamide hydrochloride |
| 90 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(4-methyl-1H-pyrazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 91 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[2-(2-pyridinylmethoxy)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 92 | +++++ | 4-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-methylbutanamide |
| 93 | +++++ | N-(allyloxy)-4-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]butanamide |
| 94 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(4-thiomorpholinyl)sulfonyl]butyl}phenyl)ethyl)benzenesulfonamide |
| 95 | +++++ | methyl ({2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl}sulfanyl)acetate |
| 96 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(methylsulfanyl)propyl]phenyl}ethyl)benzenesulfonamide |
| 97 | +++++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 4-thiomorpholinecarboxylate |
| 98 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-tetraazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 99 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[methoxy(methyl)amino]butyl}phenyl)ethyl]benzenesulfonamide |
| 100 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-tetraazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 101 | +++++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-[2-(4-morpholinyl)ethyl]propanamide |
| 102 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[4-fluoro-2-(4-oxopentyl)phenyl]ethyl)benzenesulfonamide |
| 103 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[4-fluoro-2-(4-oxobutyl)phenyl]ethyl)benzenesulfonamide |
| 104 | +++++ | 4-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-ethoxybutanamide |
| 105 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 106 | +++++ | 4-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-ethylbutanamide |
| 107 | +++++ | methyl 3-({2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl}sulfonyl)propanoate |
| 108 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-oxo-3-(4-thiomorpholinyl)propyl]phenyl}ethyl)benzenesulfonamide |
| 109 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{3-[methyl(methylsulfanyl)amino]propoxy}phenyl)ethyl]benzenesulfonamide |
| 110 | +++++ | N-{3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylnicotinamide hydrochloride |
| 111 | +++++ | 4-chloro-N-[(1R)-1-(2-{3-[(diethylamino)sulfonyl]propyl}-4-fluorophenyl)ethyl]-N-(2,5-difluorophenyl)benzenesulfonamide |
| 112 | +++++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-isobutylpropanamide |
| 113 | +++++ | methyl 2-amino-3-{{2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl}sulfonyl}propanoate hydrochloride |
| 114 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[4-fluoro-2-(5,5,5-trifluoro-4-oxopentyl)phenyl]ethyl)benzenesulfonamide |
| 115 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(ethylsulfanyl)ethyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 116 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(4-methyl-1-piperazinyl)propyl]phenyl}ethyl)benzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 117 | +++++ | 3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-(tetrahydro-2-furanylmethyl)propanamide |
| 118 | +++++ | 3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-cyclohexylpropanamide |
| 119 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(2-[3-(2-methyl-1H-imidazol-1-yl)propoxy]phenyl)ethyl)benzenesulfonamide hydrochloride |
| 120 | +++++ | 3-((2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]ethyl)sulfonyl)propanoic acid |
| 121 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(2-[3-(2,5-dioxo-1-pyrrolidinyl)propoxy]phenyl)ethyl)benzenesulfonamide |
| 122 | +++++ | 3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]propyl 4-thiomorpholinecarboxylate |
| 123 | +++++ | tert-butyl 4-{3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]propanoyl}-1-piperazinecarboxylate |
| 124 | +++++ | N-{4-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]butyl}-N-methylpropanamide |
| 125 | +++++ | 4-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-cyclohexylbutanamide |
| 126 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(2-[4-(ethylsulfonyl)butyl]-4-fluorophenyl)ethyl)benzenesulfonamide |
| 127 | +++++ | 3-((2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl)sulfonyl)propanoic acid |
| 128 | +++++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]ethyl nicotinate hydrochloride |
| 129 | +++++ | N-[2-(4-chlorophenyl)ethyl]-3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]propanamide |
| 130 | +++++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N,2,2-trimethylpropanamide |
| 131 | +++++ | methyl ((2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]ethyl)sulfonyl)acetate |
| 132 | +++++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]ethyl 4-thiomorpholinecarboxylate |
| 133 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(4-fluoro-2-[3-(1H-imidazol-1-yl)butyl]phenyl)ethyl)benzenesulfonamide hydrochloride |
| 134 | +++++ | 4-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-isobutoxybutanamide |
| 135 | +++++ | 1-tert-butyl 4-{2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]ethyl} 1,4-piperazinecarboxylate |
| 136 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(4-fluoro-2-[3-(4-morpholinyl)-3-oxopropyl]phenyl)ethyl)benzenesulfonamide |
| 137 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(2-[3-(4-methyl-1-piperazinyl)-3-oxopropyl]phenyl)ethyl)benzenesulfonamide |
| 138 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(4-fluoro-2-((3E)-3-(hydroxyimino)butyl)phenyl)ethyl)benzenesulfonamide |
| 139 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 140 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide |
| 141 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 142 | +++++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl nicotinate |
| 143 | +++++ | 4-[2-((1R)-1-(2,5-dichloro[(4-chlorophenyl)sulfonyl]anilino)ethyl)-5-fluorophenyl]butanoic acid |
| 144 | +++++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl 4-morpholinecarboxylate |
| 145 | +++++ | 4-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]-N-methylbutanamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 146 | +++++ | N-benzyl-3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-[2-(dimethylamino)ethyl]propanamide |
| 147 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(2H-tetrazol-2-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 148 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[4-(methylsulfonyl)butyl]phenyl}ethyl)benzenesulfonamide |
| 149 | +++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[(methylamino)sulfonyl]butyl}phenyl)ethyl]benzenesulfonamide |
| 150 | +++++ | 3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-[3-(1H-imidazol-1-yl)propyl]propanamide |
| 151 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1-piperidinyl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 152 | +++++ | 2-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]ethyl 3-pyridinylmethylcarbamate |
| 153 | +++++ | N-butyl-3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-methylpropanamide |
| 154 | +++++ | 2-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]ethyl isonicotinate |
| 155 | +++++ | 3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-[2-(2-pyridinyl)ethyl]propanamide |
| 156 | +++++ | N-benzyl-3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]propanamide |
| 157 | +++++ | 3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-(3-fluorobenzyl)propanamide |
| 158 | +++++ | methyl (2R)-2-amino-3-((3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl)isonicotinate |
| 159 | +++++ | 2-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl isonicotinate |
| 160 | +++++ | N-(1,3-benzodioxol-5-ylmethyl)-3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]propanamide |
| 161 | +++++ | N-(tert-butyl)-3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]propanamide |
| 162 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(5-fluoro-2-[3-(1-piperidinyl)propoxy]benzyl)benzenesulfonamide hydrochloride |
| 163 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-[3-[2-(trifluoromethyl)-1H-imidazol-1-yl]propyl]phenyl)ethyl]benzenesulfonamide |
| 164 | +++++ | 3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-(2-furylmethyl)propanamide |
| 165 | +++++ | 4-chloro-N-(2,4-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 166 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(2H-tetrazol-2-yl)ethyl]phenyl}ethyl)benzenesulfonamide |
| 167 | +++++ | 3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-[2-(diethylamino)ethyl]propanamide |
| 168 | +++++ | 3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-(2-pyridinylmethyl)propanamide |
| 169 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1S)-1-{2-[3-(1-piperidinyl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 170 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 171 | +++++ | 3-[2-((1R)-1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorophenyl]-N-(4-methylcyclohexyl)propanamide |
| 172 | +++++ | N-{2-[2-(1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N,2-dimethylpropanamide |
| 173 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[4-fluoro-2-(3-oxobutyl)phenyl]ethyl)benzenesulfonamide |
| 174 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-tetrazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 175 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 176 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-tetrazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide |
| 177 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-pyrrolidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 178 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-pyrrolidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 179 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-phenylethyl]benzenesulfonamide |
| 180 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-piperidinyl)propyl]benzyl}benzenesulfonamide hydrochloride |
| 181 | +++++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 2-(4-morpholinyl)ethylcarbamate |
| 182 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[4-fluoro-2-(5,5,5-trifluoro-4-hydroxypentyl)phenyl]ethyl)benzenesulfonamide |
| 183 | ++++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]-N-[2-(1H-indol-3-yl)ethyl]propanamide |
| 184 | ++++ | N-[1-(2-{4-[(aminocarbonyl)(methyl)amino]butoxy}phenyl)ethyl]-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 185 | ++++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)benzyl 4-morpholinecarboxylate |
| 186 | ++++ | 3-[3-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]propanoic acid |
| 187 | ++++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]-N-(3-pyridinylmethyl)propanamide |
| 188 | ++++ | 4-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]-N-methoxybutanamide |
| 189 | ++++ | methyl (2S)-2-[(tert-butoxycarbonyl)amino]-3-{[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl]sulfonyl}propanoate |
| 190 | ++++ | 4-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]methyl)-5-fluorophenyl]butanoic acid |
| 191 | ++++ | N-{3-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N-methylnicotinamide |
| 192 | ++++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]-N-(3-pyridinyl)propanamide |
| 193 | ++++ | N-{4-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-N-methylpropanamide |
| 194 | ++++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 4-morpholinecarboxylate |
| 195 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-3-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 196 | ++++ | 4-chloro-N-((1R)-1-[2-(3-cyanopropyl)-4-fluorophenyl]ethyl)-N-(2,5-difluorophenyl)benzenesulfonamide |
| 197 | ++++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 2-(2-pyridinyl)ethylcarbamate |
| 198 | ++++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 3-pyridinylcarbamate |
| 199 | ++++ | 4-chloro-N-(4-fluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 200 | ++++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl isonicotinate |
| 201 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(4-morpholinyl)-3-oxopropyl]phenyl}ethyl)benzenesulfonamide |
| 202 | ++++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl nicotinate |
| 203 | ++++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]-N-(2-methoxyethyl)propanamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 204 | ++++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 1 piperidinecarboxylate |
| 205 | ++++ | 4-[3-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]butanoic acid |
| 206 | ++++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-(4-fluorobenzyl)propanamide |
| 207 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{{(1R)-1-[4-fluoro-2-(5-methyl-4-oxo-5-hexenyl)phenyl]ethyl}benzenesulfonamide |
| 208 | ++++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 2-phenylpropylcarbamate |
| 209 | ++++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl tert-butylcarbamate |
| 210 | ++++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-[4-(trifluoromethyl)benzyl]propanamide |
| 211 | ++++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N,N-diethylpropanamide |
| 212 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{3-[[[(ethylamino)carbonyl](methylamino)propoxy]phenyl]ethyl}benzenesulfonamide |
| 213 | ++++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-2-methoxy-N-methylacetamide |
| 214 | ++++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methylacrylamide |
| 215 | ++++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 3-(1H-imidazol-1-yl)propylcarbamate |
| 216 | ++++ | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-N-methylnicotinamide |
| 217 | ++++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylacetamide |
| 218 | ++++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl isopropylcarbamate |
| 219 | ++++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl benzylcarbamate |
| 220 | ++++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-methylacetamide |
| 221 | ++++ | 4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butanoic acid |
| 222 | ++++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-methyl-4-morpholinecarboxamide |
| 223 | ++++ | 4-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N,N-diethylbutanamide |
| 224 | ++++ | methyl 4-{{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}(methylamino)-4-oxobutanoate |
| 225 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-{{(1,1-dioxido-4-thiomorpholinyl)methyl}-4-fluorophenyl}ethyl)benzenesulfonamide |
| 226 | ++++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl 4-methyl-1-piperazinecarboxylate |
| 227 | ++++ | N,N-diallyl-3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]propanamide |
| 228 | ++++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-(2,2-dimethoxyethyl)propanamide |
| 229 | ++++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-(2-phenylpropyl)propanamide |
| 230 | ++++ | 4-chloro-N-(2,5-dibromophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 231 | ++++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}acetamide |
| 232 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(3-{methyl[(methylamino)carbonyl]amino}propoxy)phenyl]ethyl}benzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 233 | ++++ | 2-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]ethyl 2-pyridinylmethylcarbamate |
| 234 | ++++ | N-{3-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl]-N-methylcyclopropanecarboxamide |
| 235 | ++++ | 2-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]ethyl 2-(2-pyridinyl)ethylcarbamate |
| 236 | ++++ | 3-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-[3-(1H-imidazol-1-yl)propyl]propanamide |
| 237 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-oxo-3-(1-piperidinyl)propyl]phenyl}ethyl)benzenesulfonamide |
| 238 | ++++ | N-{3-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}nicotinamide |
| 239 | ++++ | methyl (2S)-2-{[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)benzyl]amino}propanoate |
| 240 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1S)-2-hydroxy-1-methylethyl]benzenesulfonamide |
| 241 | ++++ | 2-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]ethyl 2-(diethylamino)ethylcarbamate |
| 242 | ++++ | 3-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-cyclooctylpropanamide |
| 243 | ++++ | 2-[[2-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl](ethyl)amino]-1,1-dimethyl-2-oxoethyl acetate |
| 244 | ++++ | N-(2-{3-[(aminocarbonyl)(methyl)amino]propoxy}benzyl)-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 245 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-1,2,3-triazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 246 | ++++ | 2-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 2,2-dimethoxyethylcarbamate |
| 247 | ++++ | 2-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]ethyl diethylcarbamate |
| 248 | ++++ | N-[5-chloro-2-(hydroxymethyl)phenyl]-4-methyl-N-[(1S)-1-methylbutyl]benzenesulfonamide |
| 249 | ++++ | tert-butyl 4-{3-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]propanoyl}-1-piperazinecarboxylate |
| 250 | ++++ | 2-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 4-methyl-1-piperazinecarboxylate |
| 251 | ++++ | N-(2,5-difluorophenyl)-4-fluoro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 252 | ++++ | 2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorobenzyl 2-pyridinecarboxylate |
| 253 | ++++ | N-{2-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}-2-methoxy-N-methylacetamide |
| 254 | ++++ | 2-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]ethyl 4-methyl-1-piperazinecarboxylate |
| 255 | ++++ | N-(tert-butyl)-3-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]propanamide |
| 256 | ++++ | 2-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 2-pyridinylmethylcarbamate |
| 257 | ++++ | 3-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-[2-(4-morpholinyl)ethyl]propanamide |
| 258 | ++++ | 4-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]-N-(3-pyridinylmethyl)butanamide hydrochloride |
| 259 | ++++ | N-[4-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl]-N-ethylacetamide |
| 260 | ++++ | N-{3-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl]-N-methyl-2-furamide |
| 261 | ++++ | N-{3-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl]-N-methylcyclobutanecarboxamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 262 | ++++ | 4-chloro-N-cyclohexyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 263 | ++++ | 4-chloro-N-cyclohexyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 264 | ++++ | 4-chloro-N-cyclohexyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 265 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{3-[[{(7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl)methyl]sulfonyl}(methyl)amino]propoxy}phenyl)ethyl]benzenesulfonamide |
| 266 | ++++ | 2-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]ethyl tetrahydro 2-furanyl)methylcarbamate |
| 267 | ++++ | 2-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl bis(2-methoxyethyl)carbamate |
| 268 | ++++ | 3-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]-N-[2-(1H-indol-3-yl)ethyl]propanamide |
| 269 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[(methylamino)sulfonyl]butyl}phenyl)ethyl]benzenesulfonamide |
| 270 | ++++ | 2-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 2-(4-morpholinyl)ethylcarbamate |
| 271 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(4,5-dihydro-1H-imidazol-2-yl)propyl]-4-fluorophenyl}ethyl)benzenesulfonamide hydrochloride |
| 272 | ++++ | 3-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-(1,2,3,4-tetrahydro-1-naphthalenyl)propanamide |
| 273 | ++++ | N-{3-[2-(1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl]-2,2-dimethylpropanamide |
| 274 | ++++ | 4-tert-butyl-N-{3-[2-(1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}benzamide |
| 275 | ++++ | 2-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]ethyl bis(2-methoxyethyl)carbamate |
| 276 | ++++ | N-{3-[2-(1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl]-N-methyl-1-adamantanecarboxamide |
| 277 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-tetrazol-5-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 278 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(4-{ethyl[(methylamino)carbonyl]amino}butoxy)phenyl]ethyl}benzenesulfonamide |
| 279 | ++++ | 2-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 1-benzyl-4-piperidinylcarbamate |
| 280 | ++++ | (2E)-3-[3-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]-2-propenoic acid |
| 281 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(4-{methyl[(methylamino)carbonyl]amino}butoxy)phenyl]ethyl}benzenesulfonamide |
| 282 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(1H-tetrazol-1-yl)methyl]phenyl)ethyl}benzenesulfonamide |
| 283 | ++++ | N-{3-[2-(1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl]-N,3-dimethyl-2-butenamide |
| 284 | ++++ | 2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)benzyl 1-piperidinecarboxylate |
| 285 | ++++ | 4-chloro-N-(2-fluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 286 | ++++ | 4-[2-((1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenyl]butanoic acid |
| 287 | ++++ | 2-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl tetrahydro-2-furanyl)methylcarbamate |
| 288 | ++++ | 3-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-(2,5-difluorobenzyl)propanamide |
| 289 | ++++ | N-(4-[[{3-[2-(1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl](methyl)amino]sulfonyl]phenyl)acetamide |
| 290 | ++++ | 3-[2-((1R)-1-[[{(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]-N-[2-(2-pyridinyl)ethyl]propanamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 291 | ++++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-ethyl-2-methoxyacetamide |
| 292 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-oxido-1-pyrrolidinyl)propoxy]benzyl}benzenesulfonamide |
| 293 | +++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N,2,2-trimethylpropanamide |
| 294 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(2-{ethyl[(methylamino)carbonyl]amino}ethoxy)phenyl]ethyl}benzenesulfonamide |
| 295 | +++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 3-pyridinylcarbamate |
| 296 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl benzyl(methyl)carbamate |
| 297 | +++ | N-[1-(2-{3-[[tert-butylamino]carbonyl](methyl)amino]propoxy}phenyl)ethyl]-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 298 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 3-(1H-imidazol-1-yl)propylcarbamate |
| 299 | +++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methylpropanamide |
| 300 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]-N-(2-pyridinylmethyl)propanamide |
| 301 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]propyl 3-(1H-imidazol-1-yl)propylcarbamate |
| 302 | +++ | 4-chloro-N-{2-[2-(cyclohexylsulfinyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |
| 303 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl diallylcarbamate |
| 304 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-(1-phenylethyl)propanamide |
| 305 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(2-methyl-1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 306 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 1,2,3,4-tetrahydro-1-naphthalenylcarbamate |
| 307 | +++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl 2-(4-morpholinyl)ethylcarbamate |
| 308 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-(phenylsulfonyl)acetamide |
| 309 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-3-cyano-N-methylbenzamide |
| 310 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]-N-(2,2-dimethoxyethyl)propanamide |
| 311 | +++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl cyclooctylcarbamate |
| 312 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl cyclooctylcarbamate |
| 313 | +++ | 4-chloro-N-(2,3-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 314 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-thiophenesulfonamide |
| 315 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]ethyl methyl(phenyl)carbamate |
| 316 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N,N-bis(2-methoxyethyl)propanamide |
| 317 | +++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 1,2,3,4-tetrahydro-1-naphthalenylcarbamate |
| 318 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]ethyl 2-(4-morpholinyl)ethylcarbamate |
| 319 | +++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methyl-4-morpholinecarboxamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 320 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,6-dimethoxybenzamide |
| 321 | +++ | N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl]phenoxy]propyl}-N-methylacetamide |
| 322 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 2-(1-methyl-2-pyrrolidinyl)ethylcarbamate |
| 323 | +++ | 2-{{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}(methylamino)-1,1-dimethyl-2-oxoethyl acetate |
| 324 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 325 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 2,2-dimethoxyethylcarbamate |
| 326 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]ethyl 1,3-benzodioxol-5-ylmethylcarbamate |
| 327 | +++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methylcyclobutanecarboxamide |
| 328 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 3-fluorobenzylcarbamate |
| 329 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-piperidinyl)propyl]benzyl}benzenesulfonamide hydrochloride |
| 330 | +++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-ethylpropanamide |
| 331 | +++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methylacetamide |
| 332 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]ethyl 2-(1-pyrrolidinyl)ethylcarbamate |
| 333 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-(3,4-difluorobenzyl)propanamide |
| 334 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 4-methylcyclohexylcarbamate |
| 335 | +++ | 3-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzoic acid |
| 336 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(1H-1,2,4-triazol-1-ylmethyl)phenyl]ethyl)benzenesulfonamide |
| 337 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-methyl-N-phenylpropanamide |
| 338 | +++ | N,N-diallyl-3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]propanamide |
| 339 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-[2-(1H-1,2,4-triazol-1-yl)ethyl]phenyl]ethyl)benzenesulfonamide |
| 340 | +++ | 4-butoxy-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}benzamide |
| 341 | +++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N,2,2-trimethylpropanamide |
| 342 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]-N-[4-(trifluoromethyl)benzyl]propanamide |
| 343 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]ethyl 2-(diethylamino)ethylcarbamate |
| 344 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-(2-thienyl)acetamide |
| 345 | +++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 2-(1H-indol-3-yl)ethylcarbamate |
| 346 | +++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl methyl(phenyl)carbamate |
| 347 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-nitro-4-(trifluoromethyl)benzenesulfonamide |
| 348 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{3-[methyl(phenylsulfonyl)amino]propoxy}phenyl)ethyl]benzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 349 | +++ | 2-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl phenylcarbamate |
| 350 | +++ | 2,6-dichloro-N-{3-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}benzamide |
| 351 | +++ | methyl 3-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl(methyl)carbamate |
| 352 | +++ | 3-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]-N-phenylpropanamide |
| 353 | +++ | 3-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(tetrahydro-2-furanyl)methylpropanamide |
| 354 | +++ | 2-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 3-(1H-imidazol-1-yl)propylcarbamate |
| 355 | +++ | N-{4-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-N-methylcyclobutanecarboxamide |
| 356 | +++ | 4-chloro-2-[[[4-chlorophenyl)sulfonyl]((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)amino]benzyl acetate |
| 357 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(4-{ethyl[(isopropylamino)carbonyl]amino}butoxy)phenyl]ethyl}benzenesulfonamide |
| 358 | +++ | 2-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 2,5-difluorobenzylcarbamate |
| 359 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[(4-pyridinylmethoxy)methyl]phenyl}ethyl)benzenesulfonamide |
| 360 | +++ | 2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 2-(diethylamino)ethylcarbamate |
| 361 | +++ | 2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl methyl(phenyl)carbamate |
| 362 | +++ | 2-chloro-N-{3-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}benzamide |
| 363 | +++ | methyl {[4-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}(methyl)amino)(oxo)acetate |
| 364 | +++ | 2-{2-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}(methyl)amino)-1,1-dimethyl-2-oxoethyl acetate |
| 365 | +++ | 2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl cyclohexylcarbamate |
| 366 | +++ | 2-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]-N-methoxyacetamide |
| 367 | +++ | N-{3-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-2-nitrobenzamide |
| 368 | +++ | 2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl phenylcarbamate |
| 369 | +++ | 2-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl methyl(phenyl)carbamate |
| 370 | +++ | 2-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 4-(trifluoromethyl)benzylcarbamate |
| 371 | +++ | 2-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl isobutylcarbamate |
| 372 | +++ | N-{4-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-N-ethyl-2,2-dimethylpropanamide |
| 373 | +++ | N-{3-[2-(1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N-methylacrylamide |
| 374 | +++ | 4-chloro-N-[1-(2-{4-[[[diethylamino]carbonyl](methyl)amino]butoxy}phenyl)ethyl]-N-(2,5-difluorophenyl)benzenesulfonamide |
| 375 | +++ | 4-chloro-N-{2-[3-(diethylamino)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide hydrochloride |
| 376 | +++ | 4-chloro-N-{2-[3-(diethylamino)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide hydrochloride |
| 377 | +++ | 3-[2-((1R)-1-[[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N,N-diethylpropanamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 378 | +++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]propyl 1-piperidinecarboxylate |
| 379 | +++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl isopropylcarbamate |
| 380 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[(3-pyridinylmethoxy)methyl]phenyl}ethyl)benzenesulfonamide |
| 381 | +++ | N-{2-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}-N-methyl-2-(2-thienyl)acetamide |
| 382 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(2-{methyl[(methylamino)carbonyl]amino}ethoxy)phenyl]ethyl}benzenesulfonamide |
| 383 | +++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(2,5-difluorobenzyl)propanamide |
| 384 | +++ | N-{4-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-N-methyl-2-(phenylsulfonyl)acetamide |
| 385 | +++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 1-phenylethylcarbamate |
| 386 | +++ | N-{3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]methyl)phenoxy]propyl}-2-methoxy-N-methylacetamide |
| 387 | +++ | N-{3-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N,4,7,7-tetramethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxamide |
| 388 | +++ | N-(1,3-benzodioxol-5-ylmethyl)-3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]propanamide |
| 389 | +++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl benzylcarbamate |
| 390 | +++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]-N-(2-phenylethyl)propanamide |
| 391 | +++ | 4-chloro-N-(2-chloro-3-pyridinyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 392 | +++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 2-methoxyethylcarbamate |
| 393 | +++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-[2-(1-pyrrolidinyl)ethyl]propanamide |
| 394 | +++ | N-{3-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N-methylcyclopentanecarboxamide |
| 395 | +++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 2,2-dimethoxyethylcarbamate |
| 396 | +++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 2-methoxyethylcarbamate |
| 397 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{2-[[[(dimethylamino)carbonyl](methyl)amino]ethoxy}phenyl]ethyl}benzenesulfonamide |
| 398 | +++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl isobutylcarbamate |
| 399 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(2,5-dioxo-1-pyrrolidinyl)propoxy]benzyl}benzenesulfonamide |
| 400 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[(2-pyridinylmethoxy)methyl]phenyl}ethyl)benzenesulfonamide |
| 401 | +++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-cyclohexylpropanamide |
| 402 | +++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 2-phenylpropylcarbamate |
| 403 | +++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-phenylpropanamide |
| 404 | +++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(2-furylmethyl)propanamide |
| 405 | +++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethanesulfonic acid |
| 406 | +++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(1,2,3,4-tetrahydro-1-naphthalenyl)propanamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 407 | +++ | 4-chloro-N-{2-[3-(cyclohexylsulfinyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |
| 408 | +++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-2,6-difluorobenzamide |
| 409 | +++ | 4-butyl-N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}benzamide |
| 410 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(3-{methyl[(4-nitrophenyl)sulfonyl]amino}propoxy)phenyl]ethyl}benzenesulfonamide |
| 411 | +++ | 3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]propyl isopropylcarbamate |
| 412 | +++ | N-{2-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}-N-ethyl-2,2-dimethylpropanamide |
| 413 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(3-hydroxypropyl)benzyl]benzenesulfonamide |
| 414 | +++ | 1-tert-butyl 4-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl] 1,4-piperazinedicarboxylate |
| 415 | +++ | methyl {[3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}(methylamino)(oxo)acetate |
| 416 | +++ | [[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)benzyl](methylamino)acetic acid hydrochloride |
| 417 | +++ | N-{2-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}-N-ethyl-2-(phenylsulfonyl)acetamide |
| 418 | +++ | 2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 2-(1-methyl-2-pyrrolidinyl)ethylcarbamate |
| 419 | +++ | 2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 4-fluorobenzylcarbamate |
| 420 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-({3-[3-(1-piperidinyl)propoxy]-2-naphthyl}methyl)benzenesulfonamide hydrochloride |
| 421 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-({3-[3-(1-piperidinyl)propoxy]-2-naphthyl}methyl)benzenesulfonamide hydrochloride |
| 422 | +++ | 2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 2-phenylethylcarbamate |
| 423 | +++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-4-propylbenzamide |
| 424 | +++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-2-methoxy-N-methylbenzamide |
| 425 | +++ | 2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl benzyl[2-(dimethylamino)ethyl]carbamate |
| 426 | +++ | 3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-methyl-N-phenylpropanamide |
| 427 | +++ | 3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(2-phenylpropyl)propanamide |
| 428 | +++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-3-cyclopentyl-N-methylpropanamide |
| 429 | +++ | 2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl tetrahydro 2-furanylmethylcarbamate |
| 430 | +++ | 3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(3,4-difluorobenzyl)propanamide |
| 431 | +++ | 3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(1-phenylethyl)propanamide |
| 432 | +++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}acrylamide |
| 433 | +++ | N-{4-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-N,3-dimethyl-2-butenamide |
| 434 | +++ | N-{2-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}-N-ethyl-2-methoxyacetamide |
| 435 | +++ | 2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl 2-furylmethylcarbamate |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 436 | +++ | 2-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]ethyl 2-(1H-indol-3-yl)ethylcarbamate |
| 437 | +++ | 2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorobenzyl isopropylcarbamate |
| 438 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(1H-imidazol-1-ylmethyl)phenyl]ethyl)benzenesulfonamide hydrochloride |
| 439 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(1H-tetrazol-1-ylmethyl)phenyl]ethyl)benzenesulfonamide |
| 440 | +++ | 4-tert-butyl-N-{3-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 441 | +++ | 2-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl butyl(methyl)carbamate |
| 442 | +++ | N-{2-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methylcyclopentanecarboxamide |
| 443 | +++ | 3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]-N-(2-phenylethyl)propanamide |
| 444 | +++ | N-benzyl-3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N-methylpropanamide |
| 445 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(4-{ethyl[(ethylamino)carbonyl]amino}butoxy)phenyl]ethyl}benzenesulfonamide |
| 446 | +++ | 3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]-N-(3-pyridinylmethyl)propanamide |
| 447 | +++ | 6-amino-N-{3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylhexanamide hydrochloride |
| 448 | +++ | 6-amino-N-{3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylhexanamide hydrochloride |
| 449 | +++ | N-{4-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-ethylcyclobutanecarboxamide |
| 450 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(2-pyridinylcarbonyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 451 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(3-pyridinylcarbonyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 452 | +++ | N-benzyl-3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]-N-methylpropanamide |
| 453 | +++ | N-{2-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-ethylacetamide |
| 454 | +++ | N-{4-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-ethyl-2-methylpropanamide |
| 455 | +++ | 2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 1-benzyl-4-piperidinylcarbamate |
| 456 | +++ | 2-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenyl]ethyl 3-pyridinylcarbamate |
| 457 | +++ | 2-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 2-phenylpropylcarbamate |
| 458 | +++ | N-{3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N,2,2-trimethylpropanamide |
| 459 | +++ | 2-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]ethyl 2-(4-chlorophenyl)ethylcarbamate |
| 460 | +++ | 4-chloro-N-(2-chlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 461 | +++ | N-{3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylpropanamide |
| 462 | +++ | N-{3-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-3-nitrobenzenesulfonamide |
| 463 | +++ | N-{4-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-methylbutanamide |
| 464 | +++ | N-{3-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2-fluorobenzamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 465 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-({3-[3-(1-piperidinyloxy)propoxy]-2-pyridinyloxy)methyl}benzenesulfonamide hydrochloride |
| 466 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 467 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoro-N-methyloctanamide |
| 468 | +++ | methyl 4-{{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}(methylamino)-4-oxobutanoate |
| 469 | +++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-methyl-2-(2-thienyl)acetamide |
| 470 | +++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-ethylbutanamide |
| 471 | +++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-4-ethyl-N-methylbenzamide |
| 472 | +++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]propyl methyl(phenyl)carbamate |
| 473 | +++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 2-(1H-indol-3-yl)ethylcarbamate |
| 474 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-methylcyclopentanecarboxamide |
| 475 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-thiophenecarboxamide |
| 476 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{{1-[2-{{3-{{(4-fluorophenyl)sulfonyl}(methylamino)propoxy}phenyl)ethyl}benzenesulfonamide |
| 477 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-1,3-benzodioxole-5-carboxamide |
| 478 | ++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]-N-(2-methoxyethyl)propanamide |
| 479 | ++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]propyl diethylcarbamate |
| 480 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl 2-(1H-indol-3-yl)ethylcarbamate |
| 481 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 3-pyridinylmethylcarbamate |
| 482 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-nitrobenzenesulfonamide |
| 483 | ++ | methyl {{2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl}amino}acetate |
| 484 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methylbutanamide |
| 485 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-ethyl-3-methylbutanamide |
| 486 | ++ | 1-tert-butyl 4-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl] 1,4-piperazinedicarboxylate |
| 487 | ++ | N-{2-(4-chlorophenyl)ethyl}-3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]propanamide |
| 488 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methylbenzamide |
| 489 | ++ | 4-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-N,N-dipropylbutanamide |
| 490 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N,3-dimethylbutanamide |
| 491 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(1H-tetrazol-1-yl)methyl]benzylbenzenesulfonamide |
| 492 | ++ | 4-chloro-N-(2-[3-(1,1-dioxido-4-thiomorpholinyl)propoxy]benzyl)-N-phenylbenzenesulfonamide hydrochloride |
| 493 | ++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]ethyl diallylcarbamate |

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|--------|----------|--|
| 494 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methyl-2-(phenylsulfanyl)acetamide |
| 495 | ++ | (2E)-N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-methyl-2-butenamide |
| 496 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}[1,1'-biphenyl]-4-carboxamide |
| 497 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,3,6-trifluorobenzamide |
| 498 | ++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]propyl benzylcarbamate |
| 499 | ++ | ethyl 4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butanoate |
| 500 | ++ | N-(sec-butyl)-3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]propanamide |
| 501 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N,3-dimethyl-2-butenamide |
| 502 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,4-difluoro-N-methylbenzamide |
| 503 | ++ | (2E)-N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methyl-2-butenamide |
| 504 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-ethylpropanamide |
| 505 | ++ | 2-bromo-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 506 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-ethyl-4-morpholinecarboxamide |
| 507 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 2,5-difluorobenzylcarbamate |
| 508 | ++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]ethyl 2,5-difluorobenzylcarbamate |
| 509 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl 3-(1H-imidazol-1-yl)propylcarbamate |
| 510 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methyl-1-adamantanecarboxamide |
| 511 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methylcyclohexanecarboxamide |
| 512 | ++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]propanamide |
| 513 | ++ | 2-chloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 514 | ++ | (2E)-N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-ethyl-2-butenamide |
| 515 | ++ | N-benzyl-3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]propanamide |
| 516 | ++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]-N-[2-(diethylamino)ethyl]propanamide |
| 517 | ++ | N-butyl-3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]-N-methylpropanamide |
| 518 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,6-dimethoxy-N-methylbenzamide |
| 519 | ++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]-N-(3-fluorobenzyl)propanamide |
| 520 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,5-difluorobenzamide |
| 521 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl bis(2-methoxyethyl)carbamate |
| 522 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N,3-dimethylbutanamide |

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|--------|----------|--|
| 523 | ++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-2,3-difluoro-N-methylbenzamide |
| 524 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(2H-tetrazol-2-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 525 | ++ | 2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 3-fluorobenzylcarbamate |
| 526 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[2-(1H-imidazol-1-yl)ethyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 527 | ++ | methyl 4-({3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}amino)-4-oxobutanoate |
| 528 | ++ | 4-butoxy-N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N-methylbenzamide |
| 529 | ++ | 2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)benzyl 3-pyridinylmethylcarbamate |
| 530 | ++ | 2-{{3-[2-((4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl]phenoxy]propyl}(methyl)amino]-1,1-dimethyl-2-oxoethyl acetate |
| 531 | ++ | 3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(3-pyridinyl)propanamide |
| 532 | ++ | 3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-isobutylpropanamide |
| 533 | ++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N-methyl-9-oxo-9H-fluorene-4-carboxamide |
| 534 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(2H-tetrazol-2-yl)methyl]phenyl)ethyl)benzenesulfonamide |
| 535 | ++ | 2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl benzyl[2-(dimethylamino)ethyl]carbamate |
| 536 | ++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-2,4-difluorobenzamide |
| 537 | ++ | 2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorophenyl]ethyl sec-butylcarbamate |
| 538 | ++ | 2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 2-(2-pyridinyl)ethylcarbamate |
| 539 | ++ | 2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 1-phenylethylcarbamate |
| 540 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{3-[methyl(4-toluidinocarbonyl)amino]propoxy}phenyl)ethyl]benzenesulfonamide |
| 541 | ++ | N-{4-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-N-ethyl-2-(2-thienyl)acetamide |
| 542 | ++ | 2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)benzyl 2-(2-pyridinyl)ethylcarbamate |
| 543 | ++ | N-[1-(2-{3-[[4-tert-butylphenyl)sulfonyl](methyl)amino]propoxy}phenyl)ethyl]-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 544 | ++ | N-benzyl-3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-[2-(dimethylamino)ethyl]propanamide |
| 545 | ++ | N-{3-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-1-naphthamide |
| 546 | ++ | 3-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]propyl butyl(methyl)carbamate |
| 547 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-(2,3,4,5,6-pentafluorophenyl)ethyl)benzenesulfonamide |
| 548 | ++ | N-{4-[2-(1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-N-ethyl-3-methyl-2-butenamide |
| 549 | ++ | 2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 3,4-difluorobenzylcarbamate |
| 550 | ++ | 2-[2-((1R)-1-[[4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl diethylcarbamate |
| 551 | ++ | N-{3-[2-((4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl]phenoxy]propyl}-N,2-dimethylpropanamide |

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|--------|----------|---|
| 552 | ++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]-N-(4-fluorobenzyl)propanamide |
| 553 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{4-[[[(ethylamino)carbonyl](methyl)amino]butoxy}phenyl)ethyl]benzenesulfonamide |
| 554 | ++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl benzyl(methyl)carbamate |
| 555 | ++ | 3-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]propyl 3,4-difluorobenzylcarbamate |
| 556 | ++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 1-piperidinecarboxylate |
| 557 | ++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 4-methylcyclohexylcarbamate |
| 558 | ++ | N-{3-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N,4-dimethyl-2-nitrobenzamide |
| 559 | ++ | N-{2-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}-N-ethyl-2-methylpropanamide |
| 560 | ++ | methyl 4-{[2-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}(ethyl)amino]-4-oxobutanoate |
| 561 | ++ | N-{4-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]butyl}-N-methylbenzamide |
| 562 | ++ | allyl 3-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl(methyl)carbamate |
| 563 | ++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)benzyl 2,2-dimethoxyethylcarbamate |
| 564 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{2-[methyl(methylsulfonyl)amino]ethoxy}phenyl)ethyl]benzenesulfonamide |
| 565 | ++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 2-(4-chlorophenyl)ethylcarbamate |
| 566 | ++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl benzyl(methyl)carbamate |
| 567 | ++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl benzylcarbamate |
| 568 | ++ | 2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)-5-fluorobenzyl 2-pyridinylmethylcarbamate |
| 569 | ++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 2-phenylethylcarbamate |
| 570 | ++ | N-{3-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-N-methyl-2-nitrobenzamide |
| 571 | ++ | N-{3-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-3,4-difluoro-N-methylbenzamide |
| 572 | ++ | 4-chloro-N-[1-(2-{2-[[[(diethylamino)carbonyl](methyl)amino]ethoxy}phenyl)ethyl]-N-(2,5-difluorophenyl)benzenesulfonamide |
| 573 | ++ | N-{2-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}-N-methyl-2-furamide |
| 574 | ++ | (2S)-2-{[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)benzyl]amino}propanoic acid |
| 575 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{3-[[4-methoxyphenyl)sulfonyl](methyl)amino]propoxy}phenyl)ethyl]benzenesulfonamide |
| 576 | ++ | 2-[2-((1R)-1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenyl]ethyl 4-fluorobenzylcarbamate |
| 577 | ++ | N-[1-(2-{4-[[[(tert-butylamino)carbonyl](ethyl)amino]butoxy}phenyl)ethyl]-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 578 | ++ | N-benzyl-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 579 | ++ | N-{2-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]ethyl}-N-methyl-2-thiophenecarboxamide |
| 580 | ++ | N-{3-[2-(1-[[4-(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl)phenoxy]propyl}-4-cyano-N-methylbenzamide |

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|--------|----------|--|
| 581 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl tetrahydro-2-furanylmethylcarbamate |
| 582 | ++ | 2,5-dichloro-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methylbenzenesulfonamide |
| 583 | ++ | 2-chloro-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methylbenzenesulfonamide |
| 584 | ++ | 4-butyl-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methylbenzamide |
| 585 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(1H-1,2,4-triazol-1-ylmethyl)benzyl]benzenesulfonamide |
| 586 | ++ | N-[1-(2-{4-[[[(tert-butylamino)carbonyl](methyl)amino]butoxy]phenyl}ethyl)-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 587 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 2-(1-methyl-2-pyrrolidinyl)ethylcarbamate |
| 588 | ++ | N-{4-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]butyl}-N-methylpentanamide |
| 589 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}benzamide |
| 590 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2-methylbenzamide |
| 591 | ++ | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethylbenzamide |
| 592 | ++ | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethyl-2-thiophenecarboxamide |
| 593 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 4-(trifluoromethyl)benzylcarbamate |
| 594 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(2-{ethyl[(ethylamino)carbonyl]amino}ethoxy)phenyl]ethyl}benzenesulfonamide |
| 595 | ++ | {[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl]amino}acetic acid hydrochloride |
| 596 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-N-methyl-4-morpholinecarboxamide |
| 597 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[[[(dimethylamino)carbonyl](methyl)amino]propoxy]benzyl}benzenesulfonamide |
| 598 | ++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl 2-(4-chlorophenyl)ethylcarbamate |
| 599 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-[2-[3-(methyl{[4-(trifluoromethyl)phenyl]sulfonyl}amino)propoxy]phenyl]ethyl)benzenesulfonamide |
| 600 | ++ | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethylcyclobutanecarboxamide |
| 601 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl diethylcarbamate |
| 602 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-4-nitrobenzamide |
| 603 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2-cyclohexyl-N-methylacetamide |
| 604 | ++ | 4-chloro-N-{2-[3-(cyclohexylsulfonyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |
| 605 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-4-cyano-N-methylbenzamide |
| 606 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-4-cyanobenzamide |
| 607 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-3,5-dinitrobenzamide |
| 608 | ++ | N-(2,5-difluorophenyl)-4-methyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 609 | ++ | N-{4-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]butyl}-N-ethylpentanamide |

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|--------|----------|--|
| 610 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 2-(1-pyrrolidinyl)ethylcarbamate |
| 611 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[6-(1-piperidinyl)hexyl]benzenesulfonamide hydrochloride |
| 612 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl isobutylcarbamate |
| 613 | ++ | tert-butyl 6-[[3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl](methyl)amino)-6-oxohexylcarbamate |
| 614 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl 1,3-benzodioxol-5-ylmethylcarbamate |
| 615 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl 4-morpholinecarboxylate |
| 616 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-3,5-difluoro-N-methylbenzamide |
| 617 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N,2,4,6-tetramethylbenzenesulfonamide |
| 618 | ++ | S-methyl 4-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]butyl(methyl)thiocarbamate |
| 619 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl 4-fluorobenzylcarbamate |
| 620 | ++ | 3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]propyl 4-fluorobenzylcarbamate |
| 621 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(3-hydroxy-1-propynyl)benzyl]benzenesulfonamide |
| 622 | ++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl (1S)-1-phenylethylcarbamate |
| 623 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2,3,6-trifluoro-N-methylbenzamide |
| 624 | ++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl butyl(methyl)carbamate |
| 625 | ++ | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethyl-2-furamide |
| 626 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl diallylcarbamate |
| 627 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-N-methylcyclohexanecarboxamide |
| 628 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-2,2-diphenylacetamide |
| 629 | ++ | 4-chloro-N-phenyl-N-{2-[3-(1-piperidinyl)propyl]benzyl}benzenesulfonamide hydrochloride |
| 630 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2-fluoro-N-methylbenzamide |
| 631 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl diallylcarbamate |
| 632 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 3-pyridinylcarbamate |
| 633 | ++ | S-methyl 3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl(methyl)thiocarbamate |
| 634 | ++ | 3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]propyl (1S)-1-phenylethylcarbamate |
| 635 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl phenylcarbamate |
| 636 | ++ | 4-chloro-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-2-nitrobenzamide |
| 637 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2-iodo-N-methylbenzamide |
| 638 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-N-methylbutanamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 639 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 2,5-difluorobenzylcarbamate |
| 640 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl 2-phenylethylcarbamate |
| 641 | ++ | 2-bromo-N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy}propyl}-N-methylbenzamide |
| 642 | ++ | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethyl-3-methyl-2-butanamide |
| 643 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-3,4-dimethoxy-N-methylbenzamide |
| 644 | ++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl 1,2,3,4-tetrahydro-1-naphthalenylcarbamate |
| 645 | ++ | 4-chloro-N-{2-[3-(4-hydroxy-1-piperidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 646 | ++ | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethylbutanamide |
| 647 | ++ | 2,4-dichloro-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methylbenzenesulfonamide |
| 648 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(4-ethoxybenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 649 | ++ | (2E)-N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethyl-2-butanamide |
| 650 | ++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl sec-butylcarbamate |
| 651 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-3,4,5-trimethoxybenzamide |
| 652 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-4-methoxy-N-methylbenzamide |
| 653 | ++ | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-3-cyclopentyl-N-methylpropanamide |
| 654 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-4-fluoro-N-methylbenzamide |
| 655 | ++ | 3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]-N-isopropylpropanamide |
| 656 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-4-propylbenzamide |
| 657 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-3-(trifluoromethyl)benzamide |
| 658 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl 4-(trifluoromethyl)benzylcarbamate |
| 659 | ++ | (2S)-2-[[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl](methyl)amino]propanoic acid hydrochloride |
| 660 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 1,2,3,4-tetrahydro-1-naphthalenylcarbamate |
| 661 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(3-fluorobenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 662 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 2-(diethylamino)ethylcarbamate |
| 663 | ++ | 4-chloro-N-(3-chlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 664 | ++ | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-methylpentanamide |
| 665 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy}propyl}-2,3-difluoro-N-methylbenzamide |
| 666 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy}propyl}-N-methyl-5-(2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide |
| 667 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 2-furylmethylcarbamate |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 668 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-3,5-dinitrobenzamide |
| 669 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl 2-methoxyethylcarbamate |
| 670 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,3,4-trifluoro-N-methylbenzamide |
| 671 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-naphthalenesulfonamide |
| 672 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(2-iodobenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 673 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl 1,3-benzodioxol-5-ylmethylcarbamate |
| 674 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl isopropylcarbamate |
| 675 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl cyclohexylcarbamate |
| 676 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-2-ethyl-N-methylhexanamide |
| 677 | ++ | isobutyl 3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl(methyl)carbamate |
| 678 | ++ | benzyl 3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl(methyl)carbamate |
| 679 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-4-fluorobenzamide |
| 680 | ++ | N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl}-N,2-dimethylbenzamide |
| 681 | ++ | 2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenyl acrylate |
| 682 | ++ | 2,4-dichloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-5-fluorobenzamide |
| 683 | ++ | 4-bromo-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 684 | ++ | 3-chloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzenesulfonamide |
| 685 | ++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenyl]ethyl cyclohexylcarbamate |
| 686 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-2-cyclohexyl-N-methylacetamide |
| 687 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-3-methylbenzamide |
| 688 | ++ | 3-chloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 689 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-nitrophenyl)sulfinyl]propoxy}benzyl)benzenesulfonamide |
| 690 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-3-methoxybenzamide |
| 691 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl 2-furylmethylcarbamate |
| 692 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{3-[(4-iodophenyl)sulfonyl](methyl)amino]propoxy}phenyl)ethyl]benzenesulfonamide |
| 693 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N,2-dimethylbenzamide |
| 694 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-ethyl-3-methylbutanamide |
| 695 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{2-[(isopropylamino)carbonyl](methyl)amino]ethoxy}phenyl)ethyl]benzenesulfonamide |
| 696 | ++ | N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl}-N,3-dimethylbenzamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 697 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-(trifluoromethyl)benzamide |
| 698 | ++ | 4-chloro-N-[1-(2-{2-[[diethylamino]carbonyl](ethyl)amino]ethoxy}phenyl)ethyl]-N-(2,5-difluorophenyl)benzenesulfonamide |
| 699 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-3-fluoro-N-methylbenzamide |
| 700 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N,2,4-trimethylpentanamide |
| 701 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(2-{methyl[(2,2,2-trifluoroethyl)sulfonyl]amino}ethoxy)phenyl)ethyl]benzenesulfonamide |
| 702 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(phenylsulfinyl)propoxy]benzyl}benzenesulfonamide |
| 703 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-4-(trifluoromethyl)benzamide |
| 704 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(2,6-dioxo-1-piperidinyl)propoxy]benzyl}benzenesulfonamide |
| 705 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-ethyl-2-(2-thienyl)acetamide |
| 706 | ++ | 4-chloro-N-(2,4-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 707 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-4-methylbenzamide |
| 708 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-ethyl-2-furamide |
| 709 | ++ | N-[1-(2-{2-[[tert-butylamino]carbonyl](ethyl)amino]ethoxy}phenyl)ethyl]-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 710 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,4,5-trifluoro-N-methylbenzamide |
| 711 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-piperidinyl)-1-propynyl]benzyl}benzenesulfonamide hydrochloride |
| 712 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-3-cyclopentyl-N-methylpropanamide |
| 713 | ++ | 2,4,6-trichloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 714 | ++ | S-methyl 4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl(ethyl)thiocarbamate |
| 715 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl benzyl(methyl)carbamate |
| 716 | ++ | N-{3-[2-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino}methyl)phenoxy]propyl}-2-iodo-N-methylbenzamide |
| 717 | ++ | N-{3-[2-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino}methyl)phenoxy]propyl}-N-methylpentanamide |
| 718 | ++ | 4-chloro-N-phenyl-N-{2-[3-(1-pyrrolidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 719 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-4-iodo-N-methylbenzamide |
| 720 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl butyl(methyl)carbamate |
| 721 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-ethylcyclopentanecarboxamide |
| 722 | ++ | 4-chloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 723 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-3-nitrobenzamide |
| 724 | ++ | N-[1-(2-{2-[[tert-butylamino]carbonyl](methyl)amino]ethoxy}phenyl)ethyl]-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 725 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{1-[2-(2-{ethyl[(isopropylamino)carbonyl]amino}ethoxy)phenyl)ethyl]benzenesulfonamide |

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|--------|----------|--|
| 726 | ++ | 2-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]ethyl 3,4-difluorobenzylcarbamate |
| 727 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2,5-difluoro-N-methylbenzamide |
| 728 | ++ | 2,4,6-trichloro-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}benzamide |
| 729 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl 2-methoxyethylcarbamate |
| 730 | ++ | 3-[2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenyl]propyl phenylcarbamate |
| 731 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 2-(4-chlorophenyl)ethylcarbamate |
| 732 | ++ | (2Z)-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-3-phenyl-2-propenamide |
| 733 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-2-fluoro-N-methylbenzamide |
| 734 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[[isopropylamino]carbonyl](methyl)amino]propoxy}benzyl)benzenesulfonamide |
| 735 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{2-[[isopropylsulfonyl](methyl)amino]ethoxy}phenyl)ethyl]benzenesulfonamide |
| 736 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2,5-bis(trifluoromethyl)benzamide |
| 737 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-3-nitrobenzamide |
| 738 | ++ | (2Z)-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-3-phenyl-2-propenamide |
| 739 | ++ | N-{4-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]butyl}-N-ethylacrylamide |
| 740 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1H-imidazol-1-yl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 741 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N,4-dimethylbenzamide |
| 742 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2,3,4,5,6-pentafluorobenzamide |
| 743 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 2-phenylethylcarbamate |
| 744 | ++ | 2,2,2-trichloro-N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethylacetamide |
| 745 | ++ | N-{2-[2-(1-benzoyl-2-piperidinyl)ethoxy]benzyl}-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 746 | ++ | 4-chloro-N-(2-{2-[1-(3,5-difluorobenzoyl)-2-piperidinyl]ethoxy}benzyl)-N-(2,5-difluorophenyl)benzenesulfonamide |
| 747 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-4-fluoro-N-methylbenzamide |
| 748 | ++ | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 4-fluorobenzylcarbamate |
| 749 | ++ | 4-chloro-N-{2-[3-(3,6-dihydro-1(2H)-pyridinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 750 | ++ | 2,4-dichloro-N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-5-fluoro-N-methylbenzamide |
| 751 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(2H-tetraazol-2-ylmethyl)benzyl]benzenesulfonamide |
| 752 | ++ | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-N-methyl[1,1'-biphenyl]-4-carboxamide |
| 753 | ++ | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2,4-dimethoxy-N-methylbenzamide |
| 754 | ++ | 4-chloro-N-{2-[2-(cyclohexylsulfonyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |

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|--------|----------|---|
| 755 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2,6-difluoro-N-methylbenzamide |
| 756 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]butyl}-N-ethyl-2-thiophenecarboxamide |
| 757 | ++ | S-ethyl 3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl(methyl)thiocarbamate |
| 758 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)benzyl sec-butylcarbamate |
| 759 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-2-phenylcyclopropanecarboxamide |
| 760 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)-5-fluorobenzyl bis(2-methoxyethyl)carbamate |
| 761 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]propyl}-3-fluorobenzamide |
| 762 | ++ | 2-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenyl]ethyl phenylcarbamate |
| 763 | ++ | 3-[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenyl]propyl benzyl(methyl)carbamate |
| 764 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)-5-fluorobenzyl 3-fluorobenzylcarbamate |
| 765 | ++ | N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl}-4-iodo-N-methylbenzamide |
| 766 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N,3-dimethylbenzamide |
| 767 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]butyl}-N-ethylbenzamide |
| 768 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]propyl}-4-ethoxy-N-methylbenzamide |
| 769 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethyl-1-adamantanecarboxamide |
| 770 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-4-(trifluoromethoxy)benzamide |
| 771 | ++ | S-methyl 2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]ethyl(ethyl)thiocarbamate |
| 772 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(1H-imidazol-1-yl)methyl]benzyl]benzenesulfonamide |
| 773 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(methyl{(E)-2-phenylethenyl)sulfonyl}amino]propoxy]phenyl}ethyl)benzenesulfonamide |
| 774 | ++ | 2-chloro-N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl}-N-methylbenzamide |
| 775 | ++ | N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl}-2-methoxy-N-methylbenzamide |
| 776 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]propyl}-N-methyl-1-naphthalenesulfonamide |
| 777 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethylpentanamide |
| 778 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)phenoxy]propyl}-2,3,4,5-tetrafluoro-N-methylbenzamide |
| 779 | ++ | methyl (2S)-2-[[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl)benzyl](methyl)amino]propanoate |
| 780 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(2-{1-[(2-phenylcyclopropyl)carbonyl]-2-piperidinyl}ethoxy)benzyl]benzenesulfonamide |
| 781 | ++ | 4-chloro-N-(1-methylbutyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 782 | ++ | 4-chloro-N-(1-methylbutyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 783 | ++ | (2E)-N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl}-N-methyl-2-butenamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 784 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,2-diphenylacetamide |
| 785 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-2-cyclohexyl-N-ethylacetamide |
| 786 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-3-methoxy-N-methylbenzamide |
| 787 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(2-fluorobenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 788 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-3-(trifluoromethyl)benzenesulfonamide |
| 789 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2-phenylcyclopropanecarboxamide |
| 790 | ++ | S-ethyl 4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl(ethyl)thiocarbamate |
| 791 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N,3-dimethylbutanamide |
| 792 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(1-naphthoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 793 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-2-ethyl-N-methylhexanamide |
| 794 | ++ | 4-chloro-N-[1-(2-{3-[[4-(4-chlorophenyl)sulfonyl](methyl)amino]propoxy}phenyl)ethyl]-N-(2,5-difluorophenyl)benzenesulfonamide |
| 795 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)-5-fluorobenzyl sec-butylcarbamate |
| 796 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-2,2,3,3,4,4,4-heptafluoro-N-methylbutanamide |
| 797 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(2,3,4-trifluorobenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 798 | ++ | methyl [[2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl](methyl)amino]acetate |
| 799 | ++ | 2-((1R)-1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)benzyl 2-phenylpropylcarbamate |
| 800 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 801 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{2-[[[(ethylamino)carbonyl](methyl)amino]ethoxy}phenyl)ethyl]benzenesulfonamide |
| 802 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-3,5-dimethoxy-N-methylbenzamide |
| 803 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[[4-methoxyphenyl)sulfonyl]propoxy}benzyl)benzenesulfonamide |
| 804 | ++ | N-(3-bromophenyl)-4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 805 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-4-nitrobenzamide |
| 806 | ++ | 3-bromo-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzenesulfonamide |
| 807 | ++ | 4-chloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-3-nitrobenzenesulfonamide |
| 808 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2-naphthamide |
| 809 | ++ | N-{2-[3-(3-hydroxy-1-pyrrolidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 810 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-naphthamide |
| 811 | ++ | 4-chloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}benzamide |
| 812 | ++ | 4-chloro-N-(2-{3-[(2R,6S)-2,6-dimethylpiperidinyl]propoxy}benzyl)-N-phenylbenzenesulfonamide hydrochloride |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 813 | ++ | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-2,4,5-trifluoro-N-methylbenzamide |
| 814 | ++ | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-3-methoxy-N-methylbenzamide |
| 815 | ++ | N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-3,5-difluorobenzamide |
| 816 | ++ | 4-chloro-N-(3,5-dichlorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 817 | ++ | 4-butoxy-N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-N-methylbenzamide |
| 818 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(phenylsulfonyl)propoxy]benzyl}benzenesulfonamide |
| 819 | ++ | N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-4-methoxybenzamide |
| 820 | ++ | 3-bromo-N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-N-methylbenzamide |
| 821 | ++ | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-N-methyl-1-naphthamide |
| 822 | ++ | 3,4-dichloro-N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-N-methylbenzenesulfonamide |
| 823 | ++ | 2-((1R)-1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}benzyl (1S)-1-phenylethylcarbamate |
| 824 | ++ | N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-4-iodobenzamide |
| 825 | ++ | 2-((1R)-1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}benzyl benzylcarbamate |
| 826 | ++ | phenyl 3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl(methyl)carbamate |
| 827 | ++ | 4-chloro-N-(cyclobutylmethyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 828 | ++ | N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-2,3,4,5,6-pentafluoro-N-methylbenzamide |
| 829 | ++ | 3-bromo-N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}benzamide |
| 830 | ++ | S-ethyl 2-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy)ethyl(ethyl)thiocarbamate |
| 831 | ++ | N-{2-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy)ethyl]-N,2-diethylhexanamide |
| 832 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(2-{1-[(2Z)-3-phenyl-2-propenoyl]-2-piperidinyl}ethoxy)benzyl]benzenesulfonamide |
| 833 | ++ | 4-chloro-N-(2-{3-[4-hydroxy-4-(trifluoromethyl)-1-piperidinyl]propoxy}benzyl)-N-phenylbenzenesulfonamide hydrochloride |
| 834 | ++ | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-2,4-dimethoxy-N-methylbenzamide |
| 835 | ++ | 4-chloro-N-cyclopentyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 836 | ++ | N-((1R)-1-[2-(3-aminopropoxy)phenyl]ethyl)-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 837 | ++ | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-2-ethyl-N-methylhexanamide |
| 838 | ++ | 2-((1R)-1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}benzyl benzyl[2-(dimethylamino)ethyl]carbamate |
| 839 | ++ | 2,4-dichloro-N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-N-methylbenzamide |
| 840 | ++ | N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-N-methyl[1,1'-biphenyl]-4-carboxamide |
| 841 | ++ | (2Z)-N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-N-methyl-3-phenyl-2-propenamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 842 | ++ | 4-chloro-N-(5-hexynyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 843 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-methylacrylamide |
| 844 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-2-cyclohexyl-N-methylacetamide |
| 845 | ++ | N-(2-{2-[1-([1,1'-biphenyl]-4-ylcarbonyl)-2-piperidinyl]ethoxy}benzyl)-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 846 | ++ | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]butyl}-N-methyl-1-adamantanecarboxamide |
| 847 | ++ | 3,4-dichloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methylbenzamide |
| 848 | ++ | 4-chloro-N-(cyclopentylmethyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 849 | ++ | 4-chloro-N-(2-{3-[[diethylamino]carbonyl](methyl)amino]propoxy}benzyl)-N-(2,5-difluorophenyl)benzenesulfonamide |
| 850 | ++ | 4-chloro-N-{2-[2-(cyclohexylsulfanyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |
| 851 | ++ | N-{2-[3-(1-azepanyl)propoxy]benzyl}-4-chloro-N-phenylbenzenesulfonamide hydrochloride |
| 852 | ++ | 4-chloro-N-cyclohexyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 853 | ++ | 2,2,2-trichloro-N-{3-[2-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}methyl)phenoxy]propyl}-N-methylacetamide |
| 854 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-N-methyltetradecanamide |
| 855 | ++ | N-[(1R)-1-(2-bromophenyl)ethyl]-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 856 | ++ | S-ethyl 2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl(methyl)thiocarbamate |
| 857 | ++ | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]ethyl}-3-cyclopentyl-N-ethylpropanamide |
| 858 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2-naphthamide |
| 859 | ++ | 4-chloro-N-{2-[3-(4-morpholinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 860 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(3-methylbenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 861 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-((1S)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 862 | ++ | N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl}-3-fluoro-N-methylbenzamide |
| 863 | ++ | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino}ethyl)phenoxy]propyl}-2,3,4,5-tetrafluorobenzamide |
| 864 | ++ | N-{3-[2-({(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)methyl)phenoxy]propyl}-2,3,4-trifluoro-N-methylbenzamide |
| 865 | ++ | 4-chloro-N-{2-[3-(2-ethyl-1-piperidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 866 | ++ | N-(2-bromophenyl)-4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 867 | ++ | 4-chloro-N-[(1R)-1-methylbutyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 868 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1S)-2-hydroxy-1-phenylethyl]benzenesulfonamide |
| 869 | ++ | 4-chloro-N-{2-[3-(cyclohexylsulfanyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |
| 870 | ++ | 4-chloro-N-{2-[3-(cyclohexylsulfanyl)propoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 871 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-[(4-methoxyphenyl)sulfonyl]propoxy}benzyl)benzenesulfonamide |
| 872 | ++ | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-N-methyl-4-nitrobenzamide |
| 873 | ++ | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-N-methyl-4-(trifluoromethoxy)benzamide |
| 874 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-vinylphenyl)ethyl]benzenesulfonamide |
| 875 | ++ | 4-chloro-N-(2-methylphenyl)-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 876 | ++ | 2,2,2-trichloroethyl 3-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl(methyl)carbamate |
| 877 | ++ | 4-chloro-N-{2-[3-(1,4-dioxo-8-azaspiro[4.5]dec-8-yl)propoxy]benzyl}-N-phenylbenzenesulfonamide |
| 878 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1-piperidiny)propoxy]phenyl}propyl)benzenesulfonamide hydrochloride |
| 879 | + | N-(2,5-difluorophenyl)-4-methoxy-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 880 | + | N-{2-[3-(4-benzyl-1-piperidiny)propoxy]benzyl}-4-chloro-N-phenylbenzenesulfonamide hydrochloride |
| 881 | + | 3-[2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl]-1-propanesulfonic acid |
| 882 | + | 4-chloro-N-{2-[3-(1H-imidazol-1-yl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 883 | + | 4-chloro-N-{2-[3-(1-hydroxy-1 λ 5-piperidin-1-yl)propoxy]benzyl}-N-phenylbenzenesulfonamide |
| 884 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(4-methylbenzoyl)-2-piperidiny]ethoxy}benzyl)benzenesulfonamide |
| 885 | + | 4-chloro-N-[1-(2-{3-[(4-chlorophenyl)sulfonyl](methyl)amino]propoxy}phenyl)ethyl]-N-(2,5-difluorophenyl)benzenesulfonamide |
| 886 | + | N-benzyl-4-chloro-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 887 | + | 4-chloro-N-(5-chloro-2-hydroxyphenyl)-N-(2-[3-(1-piperidiny)propoxy]benzyl)benzenesulfonamide hydrochloride |
| 888 | + | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-{2-[(diisopropylamino)carbonyl](methyl)amino]ethoxy}phenyl)ethyl]benzenesulfonamide |
| 889 | + | 4-chloro-N-{2-[2-(1-methyl-2-piperidiny)ethoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 890 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(3,4-dimethoxybenzoyl)-2-piperidiny]ethoxy}benzyl)benzenesulfonamide |
| 891 | + | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-N-methyl-3-(trifluoromethyl)benzamide |
| 892 | + | N-{3-[2-(1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)phenoxy]propyl}-N-methyl-2,5-bis(trifluoromethyl)benzamide |
| 893 | + | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-N,4-dimethylbenzamide |
| 894 | + | 2-((1R)-1-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)benzyl dicanylcarbamate |
| 895 | + | 4-chloro-N-(3-fluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 896 | + | 2,4-dichloro-N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-5-fluoro-N-methylbenzamide |
| 897 | + | 4-chloro-N-cycloheptyl-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 898 | + | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-N-methyl-4-(trifluoromethyl)benzamide |
| 899 | + | N-(2-{2-[1-(4-butoxybenzoyl)-2-piperidiny]ethoxy}benzyl)-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 900 | + | 3-chloro-N-{3-[2-(1-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}benzamide |
| 901 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(4-iodobenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 902 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(2-methoxybenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 903 | + | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-N-methyl-1,3-benzodioxole-5-carboxamide |
| 904 | + | (2S)-2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)-2-phenylethyl isonicotinate |
| 905 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{3-((4-nitrophenyl)sulfonyl)propoxy}benzyl)benzenesulfonamide |
| 906 | + | 4-chloro-N-(2,5-dichloro-3-pyridinyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 907 | + | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-N,4-dimethyl-3-nitrobenzamide |
| 908 | + | 4-chloro-N-(2,6-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 909 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(3-methoxybenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 910 | + | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)benzyl 3-fluorobenzylcarbamate |
| 911 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-[3-(1H-imidazol-1-yl)propoxy]-6-methoxybenzyl)benzenesulfonamide hydrochloride |
| 912 | + | N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(methylsulfanyl)propyl]phenyl}ethyl)-4-(methylsulfanyl)benzenesulfonamide |
| 913 | + | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-3,4,5-trimethoxy-N-methylbenzamide |
| 914 | + | 2-((1R)-1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)-5-fluorobenzyl 2-(1-pyrrolidinyl)ethylcarbamate |
| 915 | + | 4-chloro-N-{2-[3-(3-hydroxy-1-piperidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 916 | + | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1,3-dioxo-1,3-dihydro-2H-isindol-2-yl)propoxy]benzyl}benzenesulfonamide |
| 917 | + | N-{3-[2-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)methyl]phenoxy]propyl}-N-methyl-2-phenylcyclopropanecarboxamide |
| 918 | + | N-{2-[3-(1-azetidiny)propoxy]benzyl}-4-chloro-N-phenylbenzenesulfonamide hydrochloride |
| 919 | + | 4-chloro-N-(3-methylphenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 920 | + | N-{3-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]propyl}-4-(trifluoromethoxy)benzamide |
| 921 | + | N-(2-{2-[1-(1,3-benzodioxol-5-ylcarbonyl)-2-piperidinyl]ethoxy}benzyl)-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 922 | + | 4-chloro-N-(2-{3-[4-(hydroxymethyl)-1-piperidinyl]propoxy}benzyl)-N-phenylbenzenesulfonamide hydrochloride |
| 923 | + | 4-chloro-N-{2-[(1E)-3-oxo-3-(1-pyrrolidinyl)-1-propenyl]benzyl}-N-phenylbenzenesulfonamide |
| 924 | + | 4-chloro-N-[2-(methylsulfanyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 925 | + | 4-chloro-N-[2-(methylsulfanyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 926 | + | 4-chloro-N-{2-[3-(3,5-dimethyl-1-piperidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 927 | + | N-{2-[3-(4-benzyl-1-piperidinyl)propoxy]benzyl}-4-chloro-N-phenylbenzenesulfonamide hydrochloride |
| 928 | + | N-{2-[2-(1-(((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino)ethyl)phenoxy]ethyl}-N-ethyltetradecanamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 929 | + | methyl {{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy}ethyl}(methyl)amino)(oxo)acetate |
| 930 | + | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy}ethyl}-N,2,4-trimethylpentanamide |
| 931 | + | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy}propyl}-N-methyl-3,5-bis(trifluoromethyl)benzamide |
| 932 | + | 3,4-dichloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy}propyl}-N-methylbenzamide |
| 933 | + | 4-chloro-N-(2-{2-[1-(2,3-difluorobenzoyl)-2-piperidinyl]ethoxy}benzyl)-N-(2,5-difluorophenyl)benzenesulfonamide |
| 934 | + | N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy}propyl}-N-methyl-3,5-bis(trifluoromethyl)benzamide |
| 935 | + | 4-[2-((1R)-1-{4-chloro-2-[[{(4-chlorophenyl)sulfonyl}(methyl)amino]phenoxy}ethyl)-5-fluorophenyl]butanoic acid |
| 936 | + | N-(2,5-difluorophenyl)-4-(ethylsulfanyl)-N-((1R)-1-{2-[3-(ethylsulfanyl)propyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 937 | + | 4-chloro-N-phenyl-N-{2-[3-(4-thiomorpholinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 938 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(3,4,5-trimethoxybenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 939 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(1-piperidinylmethyl)phenyl]ethyl)benzenesulfonamide hydrochloride |
| 940 | + | 4-[2-(2-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)-1-methylethyl}-5-fluorophenyl]butanoic acid |
| 941 | + | 4-chloro-N-(2-{{(2S)-7-methyl-7-azabicyclo[2.2.1]hept-2-yl}methoxy}benzyl)-N-phenylbenzenesulfonamide hydrochloride |
| 942 | + | N-(2-{2-[1-(2-bromobenzoyl)-2-piperidinyl]ethoxy}benzyl)-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 943 | + | N-{4-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy]butyl}-3-cyclopentyl-N-ethylpropanamide |
| 944 | + | 4-chloro-N-phenyl-N-(2-{3-(1-piperazinyl)propoxy}benzyl)benzenesulfonamide dihydrochloride |
| 945 | + | 4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl}-N-(3-pyridinylmethyl)benzenesulfonamide hydrochloride |
| 946 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-{2-[1-(4-fluorobenzoyl)-2-piperidinyl]ethoxy}benzyl)benzenesulfonamide |
| 947 | + | 4-chloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy}propyl}-2-nitrobenzamide |
| 948 | + | 2-chloro-6-{2-[3-(1-piperidinyl)propoxy]benzyl}-6H-dibenzo[c,e][1,2]thiazine 5,5-dioxide hydrochloride |
| 949 | + | N-{2-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy}ethyl}-N-ethylacrylamide |
| 950 | + | 3,5-dichloro-N-{3-[2-(1-{{(4-chlorophenyl)sulfonyl}-2,5-difluoroanilino)ethyl}phenoxy}propyl}-N-methylbenzamide |
| 951 | + | 4-chloro-N-(4-methylpentyl)-N-(2-{3-(1-piperidinyl)propoxy}benzyl)benzenesulfonamide hydrochloride |
| 952 | + | 4-chloro-N-{3-(methylsulfanyl)phenyl}-N-(2-{3-(1-piperidinyl)propoxy}benzyl)benzenesulfonamide hydrochloride |
| 953 | + | 4-chloro-N-{3-(methylsulfanyl)phenyl}-N-(2-{3-(1-piperidinyl)propoxy}benzyl)benzenesulfonamide hydrochloride |
| 954 | + | N-((2S)-bicyclo[2.2.1]hept-2-yl)-4-chloro-N-(2-{3-(1-piperidinyl)propoxy}benzyl)benzenesulfonamide hydrochloride |
| 955 | + | 4-chloro-N-(2-methyl-2-propenyl)-N-(2-{3-(1-piperidinyl)propoxy}benzyl)benzenesulfonamide hydrochloride |
| 956 | + | 4-chloro-N-phenyl-N-(2-{3-[3-(1-piperidinyl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 957 | + | 4-chloro-N-(2,5-difluorophenyl)-N-{5-methyl-2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 958 | + | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-N-methyl-3,5-dinitrobenzamide |
| 959 | + | N-{4-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy)butyl]-N-ethylcyclopropanecarboxamide |
| 960 | + | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-3,4-dimethoxy-N-methylbenzamide |
| 961 | + | 2-((1R)-1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}benzyl 3,4-difluorobenzylcarbamate |
| 962 | + | 4-chloro-N-{2-[2-(1-methyl-2-pyrrolidinyl)ethoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 963 | + | 4-chloro-N-phenyl-N-{2-[2-(2-piperidiny)ethoxy]benzyl}benzenesulfonamide hydrochloride |
| 964 | + | 4-chloro-N-{5-chloro-2-[3-(1-piperidiny)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 965 | + | 4-chloro-N-{2-[3-(4-hydroxy-4-methyl-1-piperidiny)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 966 | + | N-{3-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy]propyl}-N-methyl-1-naphthamide |
| 967 | + | 4-chloro-N-{2-[3-(1-piperidiny)propoxy]benzyl}-N-(4-pyridinylmethyl)benzenesulfonamide dihydrochloride |
| 968 | + | 4-chloro-N-{2-[3-(4-oxo-1-piperidiny)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 969 | + | N-[(2S)-bicyclo[2.2.1]hept-2-yl]-4-chloro-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 970 | + | 4-chloro-N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-N-methylbenzamide |
| 971 | + | ethyl (2E)-3-[2-({[(4-chlorophenyl)sulfonyl]anilino)methyl}phenyl]-2-propenoate |
| 972 | + | 4-chloro-N-phenyl-N-(2-{2-[3-(1-piperidiny)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 973 | + | 4-chloro-N-phenyl-N-{2-[4-(1-piperidiny)-1-butyryl]benzyl}benzenesulfonamide |
| 974 | + | 4-chloro-N-(2,3,4,5,6-pentafluorobenzyl)-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 975 | + | 4-chloro-N-(5-chloro-2-hydroxybenzyl)-N-phenylbenzenesulfonamide |
| 976 | + | 4-chloro-N-phenyl-N-(2-{[5-(1-piperidiny)pentyl]oxy}benzyl)benzenesulfonamide hydrochloride |
| 977 | + | 4-chloro-N-phenyl-N-{2-[4-(1-piperidiny)butoxy]benzyl}benzenesulfonamide hydrochloride |
| 978 | + | 4-chloro-N-phenyl-N-{2-[5-(1-piperidiny)pentyl]benzyl}benzenesulfonamide hydrochloride |
| 979 | + | 4-chloro-N-{2-[3-(cyclopropylamino)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 980 | + | 4-chloro-N-[(1R)-1-methylbutyl]-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 981 | + | 4-chloro-N-phenyl-N-{2-[4-(1-piperidiny)butyl]benzyl}benzenesulfonamide hydrochloride |
| 982 | + | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(phenylsulfanyl)propoxy]benzyl}benzenesulfonamide |
| 983 | + | S-methyl 2-[2-(1-{{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl}phenoxy)ethyl(methyl)thiocarbamate |
| 984 | + | 4-chloro-N-(cyclopropylmethyl)-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 985 | + | N-allyl-4-chloro-N-{2-[3-(1-piperidiny)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 986 | + | 4-chloro-N-{2-[3-(1-piperidiny)propoxy]benzyl}-N-tetrahydro-2H-pyran-4-ylbenzenesulfonamide hydrochloride |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 987 | + | methyl (2S)-{[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}(phenyl)ethanoate |
| 988 | + | N-(4-bromophenyl)-4-chloro-N-{2-[3-(1-piperidinyl)propoxy]benzyl} benzenesulfonamide hydrochloride |
| 989 | + | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-3,4,5-trimethoxy-N-methylbenzamide |
| 990 | + | 4-chloro-N-{5-chloro-2-[4-(1-piperidinyl)-1-butynyl]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 991 | + | 4-chloro-N-(2-ethynylbenzyl)-N-phenylbenzenesulfonamide |
| 992 | + | N-(2,5-dichlorophenyl)(phenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}methanesulfonamide hydrochloride |
| 993 | + | 3-(2-({[(phenylsulfonyl)anilino]methyl}phenyl)propanoic acid |
| 994 | + | (E)-N-(2,5-dichlorophenyl)-2-phenyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}ethenesulfonamide hydrochloride |
| 995 | + | ethyl 3-(2-({[(phenylsulfonyl)anilino]methyl}phenyl)propanoate |
| 996 | + | 4-chloro-N-{2-[3-(cyclohexylamino)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 997 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-[3-({(4-nitrophenyl)sulfonyl}propoxy)benzyl]benzenesulfonamide |
| 998 | + | 4-chloro-N-(4-nitrobenzyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 999 | + | 4-chloro-N-{2-[3-(3,4-dihydro-2(1H)-isoquinolinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide |
| 1000 | + | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-3,5-difluoro-N-methylbenzamide |
| 1001 | + | N-[2-(allyloxy)benzyl]-4-chloro-N-phenylbenzenesulfonamide |
| 1002 | + | 3,5-dichloro-N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-N-methylbenzamide |
| 1003 | + | 4-chloro-N-cyclopropyl-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 1004 | + | 2-({[(4-chlorophenyl)sulfonyl]anilino}methyl)phenyl trifluoromethanesulfonate |
| 1005 | + | N-phenyl-N-{2-[4-(1-piperidinyl)butyl]benzyl}benzenesulfonamide |
| 1006 | + | (2S)-2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}-2-phenylethyl nicotinate |
| 1007 | + | 3-((4R)-4-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}-7-fluoro-1,2,3,4-tetrahydro-1-naphthalenyl)propanoic acid |
| 1008 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{4-fluoro-2-[3-(1,4,5,6-tetrahydro-2-pyrimidinyl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 1009 | + | [2-((1R)-1-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}ethyl)-5-fluorophenyl)methanesulfonic acid |
| 1010 | + | N-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}methyl)phenoxy]propyl}-4-ethoxy-N-methylbenzamide |
| 1011 | + | 4-chloro-N-{5-chloro-2-[3-(4-hydroxy-1-piperidinyl)propoxy]benzyl}-N-phenylbenzenesulfonamide hydrochloride |
| 1012 | + | 4-chloro-N-(2,3-dihydro-1H-inden-1-yl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 1013 | + | (2R)-2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino}propanoic acid |
| 1014 | + | S-{3-[2-({[(4-chlorophenyl)sulfonyl]anilino}methyl)phenoxy]propyl} ethanethioate |
| 1015 | + | 4-chloro-N-[2-(2-hydroxyphenyl)ethyl]-N-phenylbenzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 1016 | + | 4-chloro-N-[2-(4-hydroxybutyl)benzyl]-N-phenylbenzenesulfonamide |
| 1017 | + | 4-chloro-N-[2-(4-hydroxybutyl)benzyl]-N-phenylbenzenesulfonamide |
| 1018 | + | 4-chloro-N-phenyl-N-[2-(3-sulfanylpropoxy)benzyl]benzenesulfonamide |
| 1019 | + | 4-chloro-N-[4-(methylsulfanyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 1020 | + | 4-chloro-N-(2,3-dihydro-1H-inden-2-yl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 1021 | + | tert-butyl 2-{2-[3-(1-piperidinyl)propoxy]phenyl}-1H-indole-1-carboxylate trifluoroacetate |
| 1022 | + | N-{5-[(2,5-dichloro{2-[3-(1-piperidinyl)propoxy]benzyl}anilino)sulfonyl]-4-methyl-1,3-thiazol-2-yl}acetamide hydrochloride |
| 1023 | + | N-{5-[(2,5-dichloro{2-[3-(1-piperidinyl)propoxy]benzyl}anilino)sulfonyl]-4-methyl-1,3-thiazol-2-yl}acetamide hydrochloride |
| 1024 | + | 2-{2-[3-(1-piperidinyl)propoxy]benzyl}-2H-naphtho[1,8-cd]isothiazole 1,1-dioxide hydrochloride |
| 1025 | + | 4-chloro-N-(2,5-difluorophenyl)-N-({2-[3-(1-piperidinyl)propoxy]-1-naphthyl)methyl}benzenesulfonamide hydrochloride |
| 1026 | + | 4-chloro-N-{2-[(5-chloropentyl)oxy]benzyl}-N-phenylbenzenesulfonamide |
| 1027 | + | 4-chloro-N-[2-(methylsulfonyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 1028 | + | tert-butyl 4-{3-[2-({[(4-chlorophenyl)sulfonyl]anilino)methyl}phenoxy]propyl}-1-piperazinecarboxylate hydrochloride |
| 1029 | + | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-[(4-methoxyphenyl)sulfonyl]propoxy]benzyl}benzenesulfonamide |
| 1030 | + | 4-chloro-N-phenyl-N-[2-(4-pyridinylmethoxy)benzyl]benzenesulfonamide hydrochloride |
| 1031 | + | N-phenyl-N-{2-[3-(1-piperidinyl)propyl]benzyl}benzenesulfonamide |
| 1032 | + | 2-{1-[(4-fluorophenyl)sulfonyl]-1H-indol-2-yl}phenyl 3-(1-piperidinyl)propyl ether trifluoroacetate |
| 1033 | + | 4-chloro-N-(2,5-difluorophenyl)-N-[2-(2-{1-[4-(trifluoromethoxy)benzoyl]-2-piperidinyl]ethoxy]benzyl}benzenesulfonamide |
| 1034 | + | (2E)-3-[2-({[(4-chlorophenyl)sulfonyl]anilino)methyl}phenyl]-N-methoxy-N-methyl-2-propenamide |
| 1035 | + | (2E)-3-[2-({[(4-chlorophenyl)sulfonyl]anilino)methyl}phenyl]-2-propenoic acid |
| 1036 | + | 4-chloro-N-[3-(methylsulfonyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 1037 | + | 1-{3-[2-({[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)methyl}phenoxy]propyl}-1-methylpiperidinium iodide |
| 1038 | + | 1-{3-[2-({2,5-dichloro[(4-chlorophenyl)sulfonyl]anilino)methyl}phenoxy]propyl}-1-methylpiperidinium iodide |
| 1039 | + | N-[2-(3-bromopropoxy)benzyl]-4-chloro-N-phenylbenzenesulfonamide |
| 1040 | + | 4-chloro-N-[2-(4-hydroxy-1-butynyl)benzyl]-N-phenylbenzenesulfonamide |
| 1041 | + | N-{2-[3-oxo-3-(1-piperidinyl)propyl]benzyl}-N-phenylbenzenesulfonamide |
| 1042 | + | N-hydroxy-3-(2-({[(phenylsulfonyl)anilino]methyl}phenyl)propanamide |
| 1043 | + | 3-chloro-1-[(4-chlorophenyl)sulfonyl]-2-{2-[3-(1-piperidinyl)propoxy]phenyl}-1H-indole trifluoroacetate |
| 1044 | + | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide |

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|--------|----------|---|
| 1045 | + | N-((1R)-1-[2-(3-bromopropoxy)phenyl]ethyl)-4-chloro-N-(2,5-difluorophenyl)benzenesulfonamide |
| 1046 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 1047 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 1048 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1S)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 1049 | + | (2R,3R)-2,3-bis[(4-methylbenzoyl)oxy]butanedioic acid compound with 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propoxy]phenyl}ethyl)benzenesulfonamide |
| 1050 | + | 4-chloro-N-{2-[2-(cyclohexylsulfinyl)ethoxy]benzyl}-N-(2,5-difluorophenyl)benzenesulfonamide |
| 1051 | + | 4-chloro-N-(2,5-difluorophenyl)-N-{2-[3-(1H-imidazol-1-yl)-1-propynyl]benzyl}benzenesulfonamide hydrochloride |
| 1052 | + | 4-chloro-N-(2,5-difluorophenyl)-N-[1-(2-hydroxyphenyl)ethyl]benzenesulfonamide |
| 1053 | + | 4-benzoyl-N-((1S)-1-{{3-[2-((4-chlorophenyl)sulfonyl)-2,5-difluoroanilino]methyl}phenoxy}propyl)(methylamino)carbonyl)-5-{5-(2-oxohexahydro- |
| 1054 | + | 4-chloro-N-(2,5-difluorophenyl)-N-(2-hydroxybenzyl)benzenesulfonamide |
| 1055 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[2-(2-hydroxyethyl)phenyl]ethyl)benzenesulfonamide |
| 1056 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-imidazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 1057 | + | (2R)-2-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]propyl]isonicotinate |
| 1058 | + | (2R)-2-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]propyl]nicotinate |
| 1059 | + | N-{3-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]phenoxy]propyl)-N,2,2-trimethylpropanamide |
| 1060 | + | ethyl (2R)-2-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]propanoate |
| 1061 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1-piperidinyloxy)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 1062 | + | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-((1R)-1-{2-[3-(1-piperidinyloxy)propoxy]phenyl}ethyl)benzenesulfonamide hydrochloride |
| 1063 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-[4-fluoro-2-(3-hydroxypropyl)phenyl]ethyl)benzenesulfonamide |
| 1064 | + | 2-[2-(1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]phenoxy]-N-methylacetamide |
| 1065 | + | methyl 3-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]propanoate |
| 1066 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[3-(1H-1,2,4-triazol-1-yl)propyl]phenyl}ethyl)benzenesulfonamide |
| 1067 | + | 4-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]butanoic acid |
| 1068 | + | 4-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]butanoic acid |
| 1069 | + | 4-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]butanoic acid |
| 1070 | + | 5-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]pentanoic acid |
| 1071 | + | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{4-[(1,1-dioxido-4-thiomorpholinyl)sulfonyl]butyl}-4-fluorophenyl)ethyl]benzenesulfonamide |
| 1072 | + | 4-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]butanoic acid |
| 1073 | + | 4-[2-((1R)-1-[[[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino]ethyl]-5-fluorophenyl]butanoic acid |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 1074 | + | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(4-fluoro-2-{4-[(methylsulfonyl)amino]butyl}phenyl)ethyl]benzenesulfonamide |
| 1075 | + | 4-chloro-N-(2,5-difluorophenyl)-N-[(1R)-1-(2-{4-[(ethylsulfonyl)amino]butyl}-4-fluorophenyl)ethyl]benzenesulfonamide |
| 1076 | + | 4-[2-((1S)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl]butanoic acid |
| 1077 | + | [{(4-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl]butanoyl)amino]oxy]acetic acid |
| 1078 | + | 4-chloro-N-(2,5-difluorophenyl)-N-((1R)-1-{2-[4-(2,2-dimethylhydrazino)-4-oxobutyl]-4-fluorophenyl}ethyl)benzenesulfonamide |
| 1079 | + | 4-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl]-N-(cyanomethoxy)butanamide |
| 1080 | + | 4-[2-((1R)-1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]-5-fluorophenyl]butanoic acid |
| 1081 | - | 4-chloro-N-(2-hydroxybenzyl)-N-phenylbenzenesulfonamide |
| 1082 | - | N-{2-[3-(dimethylamino)propoxy]benzyl}-N-phenylmethanesulfonamide |
| 1083 | - | N-{2-[3-(dimethylamino)propoxy]benzyl}-4-nitro-N-phenylbenzenesulfonamide |
| 1084 | - | N-{2-[3-(dimethylamino)propoxy]benzyl}-2-nitro-N-phenylbenzenesulfonamide |
| 1085 | - | 5-(dimethylamino)-N-{2-[3-(dimethylamino)propoxy]benzyl}-N-phenyl-1-naphthalenesulfonamide |
| 1086 | - | 4-chloro-N-[2-(3-hydroxy-3-methyl-1-butynyl)benzyl]-N-phenylbenzenesulfonamide |
| 1087 | - | 4-chloro-N-phenyl-N-{2-[(trimethylsilyl)ethynyl]benzyl}benzenesulfonamide |
| 1088 | - | N-[2-(3-hydroxypropyl)benzyl]-N-phenylbenzenesulfonamide |
| 1089 | - | 4-chloro-N-[5-chloro-2-(4-hydroxy-1-butynyl)benzyl]-N-phenylbenzenesulfonamide |
| 1090 | - | 4-chloro-2-([(4-chlorophenyl)sulfonyl]anilino)methyl)phenyl trifluoromethanesulfonate |
| 1091 | - | 4-chloro-N-phenyl-N-[2-(3-pyridinylmethoxy)benzyl]benzenesulfonamide hydrochloride |
| 1092 | - | 4-chloro-N-phenyl-N-[2-(2-pyridinylmethoxy)benzyl]benzenesulfonamide hydrochloride |
| 1093 | - | (2E)-N-(benzyloxy)-3-[2-([(4-chlorophenyl)sulfonyl]anilino)methyl)phenyl]-2-propenamide hydrochloride |
| 1094 | - | 4-chloro-N-[4-(methylsulfonyl)phenyl]-N-{2-[3-(1-piperidinyl)propoxy]benzyl}benzenesulfonamide hydrochloride |
| 1095 | - | N-(2,5-difluorophenyl)-4-(phenylsulfanyl)-N-{2-[3-(phenylsulfanyl)propoxy]benzyl}benzenesulfonamide |
| 1096 | - | ethyl 4-[2-([(2-nitrophenyl)sulfonyl]anilino)methyl)phenyl]butanoate |
| 1097 | - | 4-[2-([(2-nitrophenyl)sulfonyl]anilino)methyl)phenyl]butanoic acid |
| 1098 | - | N-{2-[2-(1-[(4-chlorophenyl)sulfonyl]-2,5-difluoroanilino)ethyl]phenoxy}ethyl}-N-methyloctadecanamide |
| 1099 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-nitro-1(R)-methylbutyl]benzenesulfonamide |
| 1100 | +++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(methylsulfonyl)amino]-1(R)-methylbutyl]benzenesulfonamide |
| 1101 | +++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(methylsulfonyl)methylamino]-1(R)-methylbutyl]benzenesulfonamide |
| 1102 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[2-[(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide |

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|--------|----------|--|
| 1103 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-(2-carboxy-3-thiazolidinyl)-1(R)-methylbutyl]benzenesulfonamide |
| 1104 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[5-(1,1-dioxido-4-thiomorpholinyl)-1(R)-methylpentyl]benzenesulfonamide |
| 1105 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-(2-methoxycarbonyl-3-thiazolidinyl)-1(R)-methylbutyl]benzenesulfonamide |
| 1106 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-(2-carboxy-3-thiazolidinyl)-1(R)-methylpentyl]benzenesulfonamide |
| 1107 | +++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-nitro-1(R)-methylbutyl]benzenesulfonamide |
| 1108 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylsulfonyl)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1109 | +++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1110 | +++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[4-nitro-1(R)-methylbutyl]benzenesulfonamide |
| 1111 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-(2-carboxy-3-thiazolidinyl)-1(R)-methylpropyl]benzenesulfonamide |
| 1112 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylpentyl]benzenesulfonamide |
| 1113 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-(acetylamino)-1(R)-methylbutyl]benzenesulfonamide |
| 1114 | ++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-(4-morpholinyl)-1-methylbutyl]benzenesulfonamide |
| 1115 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(3-methylsulfonyl)-1-piperidinyl]-1(R)-methylpentyl]benzenesulfonamide |
| 1116 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[2-[(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylpentyl]benzenesulfonamide |
| 1117 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[5-(2-methoxycarbonyl-3-thiazolidinyl)-1(R)-methylpentyl]benzenesulfonamide |
| 1118 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylsulfonyl)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide |
| 1119 | ++++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-(2-methoxycarbonyl-3-thiazolidinyl)-1(R)-methylpropyl]benzenesulfonamide |
| 1120 | ++++ | 4-chloro-N-(2,5-difluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide |
| 1121 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[2-[(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1122 | +++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide |
| 1123 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylpentyl]benzenesulfonamide |
| 1124 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(S)hydroxy]phenylmethyl]carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide |
| 1125 | +++ | 4-chloro-N-(2,5-difluorophenyl)-N-[3-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide |
| 1126 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1127 | +++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[3-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide |
| 1128 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylbutyl]benzenesulfonamide |
| 1129 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[(R)hydroxy]phenylmethyl]carbonyl]amino]-1(R)-methylbutyl]benzenesulfonamide |
| 1130 | +++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[3-[2-[4-chloro-N-(5-chloro-2-fluorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-1-cyclobutenyl]amine-1(R)-methylbutyl]benzenesulfonamide |
| 1131 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[[methoxy]carbonyl]amino]-1-methylbutyl]benzenesulfonamide |

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|--------|----------|--|
| 1132 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylsulfonyl)-1-pyrrolidinyl]-1(R)-methylpropyl]benzenesulfonamide |
| 1133 | +++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-(2-methoxycarbonyl-3-thiazolidinyl)-1(R)-methylpropyl]benzenesulfonamide |
| 1134 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylthio)-1-pyrrolidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1135 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-4-[[N-(cyclopropylmethyl)-N-[3-(1H-imidazol-1-yl)propyl]amino]-1(R)-methylbutyl]benzenesulfonamide |
| 1136 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[3-[(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1137 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[1,1-dimethylethyl]carbonyl]amino]-1-methylbutyl]benzenesulfonamide |
| 1138 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-(azido)-1-methylbutyl]benzenesulfonamide |
| 1139 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[3-[2-[4-chloro-N-(2,5-difluorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-1-cyclobutenyl]amine-1(R)- |
| 1140 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[3-[(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylpentyl]benzenesulfonamide |
| 1141 | ++ | 4-chloro-N-(2,5-difluorophenyl)-N-[3-(2-isopropoxy-3,4-dioxo-1-cyclobutenyl)amine-1(R)-methylpropyl]benzenesulfonamide |
| 1142 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylthio)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide |
| 1143 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[2-[4-chloro-N-(2,5-dichlorophenyl)-N-[(3-amino)-1(R)-methylpropyl]benzenesulfonamide]-3,4-dioxo-1-cyclobutenyl]amine-1(R)- |
| 1144 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(4-methylthio)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1145 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[[1,1-dimethylethoxy]carbonyl]amino]-1-methylbutyl]benzenesulfonamide |
| 1146 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(4-methylsulfonyl)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide |
| 1147 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylthio)-1-pyrrolidinyl]-1(R)-methylpropyl]benzenesulfonamide |
| 1148 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[3-[(methylthio)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1149 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(phenyl)carbonyl]amino]-1-methylbutyl]benzenesulfonamide |
| 1150 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[5-[4-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylpentyl]benzenesulfonamide |
| 1151 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide |
| 1152 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-(4-amino)-1-methylbutyl]benzenesulfonamide |
| 1153 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(3-methylthio)-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1154 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(phenoxy)carbonyl]amino]-1-methylbutyl]benzenesulfonamide |
| 1155 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[(benzoxy)carbonyl]amino]-1-methylbutyl]benzenesulfonamide |
| 1156 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(4-methylthio)-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide |
| 1157 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[4-(methylsulfonyl)methyl]-1-piperidinyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1158 | + | 4-chloro-N-(2,5-dichlorophenyl)-N-[4-[N-(2,5-dichlorophenyl)-N-[(4-chlorophenyl)sulfonyl]amino]-1(R)-methylbutyl]benzenesulfonamide |
| 1159 | + | 4-chloro-N-(2,5-dichlorophenyl)-N-[3-[(3-methylthio)methyl]-1-piperidinyl]-1(R)-methylpropyl]benzenesulfonamide |
| 1160 | +++++ | 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-ethylsulfinyl)butyl]benzenesulfonamide |

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|--------|----------|--|
| 1161 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfonyl]butyl)]benzenesulfonamide |
| 1162 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl)]benzenesulfonamide |
| 1163 | +++++ | 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl)]benzenesulfonamide |
| 1164 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl)]benzenesulfonamide |
| 1165 | +++++ | 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl)]benzenesulfonamide |
| 1166 | +++++ | 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl)]benzenesulfonamide |
| 1167 | +++++ | 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl)]benzenesulfonamide |
| 1168 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(5-ethylsulfonyl)pentyl)]benzenesulfonamide |
| 1169 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfinyl]butyl)]benzenesulfonamide |
| 1170 | +++++ | 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl)]benzenesulfonamide |
| 1171 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl)]benzenesulfonamide |
| 1172 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-ethylsulfinyl)butyl)]benzenesulfonamide |
| 1173 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(5-ethylsulfinyl)pentyl)]benzenesulfonamide |
| 1174 | +++++ | 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-ethylsulfinyl)butyl)]benzenesulfonamide |
| 1175 | +++++ | 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl)]benzenesulfonamide |
| 1176 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-methylthio)butyl)]benzenesulfonamide |
| 1177 | +++++ | 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-ethylthio)butyl)]benzenesulfonamide |
| 1178 | +++++ | 4-chloro-N-[5-chloro-2-fluorophenyl]-N-[1(R)-methyl-(4-methylthio)butyl)]benzenesulfonamide |
| 1179 | +++++ | 4-chloro-N-[2,5-difluorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfinyl]butyl)]benzenesulfonamide |
| 1180 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(3-ethylsulfonyl)propyl)]benzenesulfonamide |
| 1181 | +++++ | (6R)-6-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]-3-thioheptanoic acid |
| 1182 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)sulfinyl]butyl)]benzenesulfonamide |
| 1183 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-ethylthio)butyl)]benzenesulfonamide |
| 1184 | ++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)sulfonyl]butyl)]benzenesulfonamide |
| 1185 | ++++ | methyl(6R)-6-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]-3-thioheptanoate |
| 1186 | ++++ | (5R)-5-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]-3-thiohexanoic acid |
| 1187 | +++ | methyl(6R)-6-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]-3-thioheptanoic acid, 3-oxide |
| 1188 | ++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(2-methylpropyl)thio)sulfonyl]butyl)]benzenesulfonamide |
| 1189 | ++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(3-ethylthio)propyl)]benzenesulfonamide |

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|--------|----------|--|
| 1190 | ++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl)]benzenesulfonamide |
| 1191 | ++ | methyl(6R)-6-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]-3-thioheptanoic acid, 3,3-dioxide |
| 1192 | ++ | (4R)-4-[N-[5-chloro-2-fluorophenyl]][(4-chlorophenyl)sulfonyl]amino]pentylsulfonic acid |
| 1193 | ++ | methyl(6R)-6-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]-3-thiohexanoic acid, 3-oxide |
| 1194 | ++ | (4R)-4-[N-[2,5-dichlorophenyl]][(4-chlorophenyl)sulfonyl]amino]pentylsulfonic acid |
| 1195 | + | methyl(4R)-4-[N-[2,5-dichlorophenyl]][(4-chlorophenyl)sulfonyl]amino]pentylsulfonate |
| 1196 | + | (6R)-6-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]-3-thioheptanoic acid, 3-oxide |
| 1197 | + | (6R)-6-[(2,5-dichlorophenyl)-[(4-chlorophenyl)sulfonyl]-amino]-3-thioheptanoic acid, 3,3-dioxide |
| 1198 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(1-azetidiny]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1199 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1200 | +++++ | 4-chloro-N-[2,5-difluorophenyl]-N-[4-[(1-azetidiny]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1201 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(dimethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1202 | +++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(dimethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1203 | +++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1204 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(1-pyrrolidinyl)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1205 | +++++ | 4-chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[(1-pyrrolidinyl)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1206 | +++++ | 4-chloro-N-[2,5-difluorophenyl]-N-[4-[(dimethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1207 | +++++ | 4-chloro-N-[2,5-difluorophenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1208 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(ethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1209 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(4-morpholinyl)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1210 | +++++ | N-[4-(aminosulfonyl)-1(R)-methylbutyl]-4-chloro-N-(2,5-dichlorophenyl)benzenesulfonamide |
| 1211 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(4-thiomorpholinyl)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1212 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[[N-(1-methylethyl)methylamino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1213 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(diethylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1214 | +++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[[[tetrahydro-1,1-dioxido-3-thienyl]amino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1215 | ++++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[[N-(cyclopentyl)methylamino]sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1216 | +++ | 4-chloro-N-[2,5-dichlorophenyl]-N-[4-[(2-methylpropylamino)sulfonyl]-1(R)-methylbutyl]benzenesulfonamide |
| 1217 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-ethylsulfonyl)butyl]benzenesulfonamide |
| 1218 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)sulfonyl]butyl]benzenesulfonamide |

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| 1219 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfinyl]butyl)benzenesulfonamide |
| 1220 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)sulfonyl]butyl)benzenesulfonamide |
| 1221 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)sulfinyl]butyl)benzenesulfonamide |
| 1222 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-ethylsulfinyl)butyl)benzenesulfonamide |
| 1223 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1-methylethyl)thio]butyl)benzenesulfonamide |
| 1224 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylsulfinyl)butyl)benzenesulfonamide |
| 1225 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl)benzenesulfonamide |
| 1226 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-phenylthio)butyl)benzenesulfonamide |
| 1227 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-ethylthio)butyl)benzenesulfonamide |
| 1228 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylthio)butyl)benzenesulfonamide |
| 1229 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-[(1,1-dimethylethyl)thio]butyl)benzenesulfonamide |
| 1230 | ++++ | 4-methylsulfonyl-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-methylsulfonyl)butyl)benzenesulfonamide |
| 1231 | ++ | (4R)-4-[N-[5-chloro-2-(hydroxymethyl)phenyl]](4-chlorophenyl)sulfonyl amino]pentylsulfonic acid |
| 1232 | + | 4-ethylthio-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[1(R)-methyl-(4-ethylthio)butyl)benzenesulfonamide |
| 1233 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(methylamino)sulfonyl]-1(R)-methylbutyl)benzenesulfonamide |
| 1234 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[(dimethylamino)sulfonyl]-1(R)-methylbutyl)benzenesulfonamide |
| 1235 | +++++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-(aminosulfonyl)-1(R)-methylbutyl)benzenesulfonamide |
| 1236 | ++ | 4-chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[4-[N-(cyclopropylmethyl)-N-[3-(1H-imidazol-1-yl)propyl]aminosulfonyl]-1(R)-methylbutyl)benzenesulfonamide |
| 1237 | +++++ | 4-Chloro-N-(2,5-dichlorophenyl)-N-[2-[[[pyrrolidin-1-yl]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1238 | +++++ | 4-Chloro-N-(2,5-difluorophenyl)-N-[2-[[[pyrrolidin-1-yl]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1239 | +++++ | 4-Chloro-N-(2,5-difluorophenyl)-N-[2-[[N'-[3-(1H-imidazol-1-yl)propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1240 | +++++ | 4-Chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-[3-(1H-imidazol-1-yl)propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1241 | +++++ | 4-Chloro-N-(2,5-dichlorophenyl)-N-[2-[[[S]-2-(hydroxymethyl)pyrrolidin-1-yl]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1242 | +++++ | 4-Chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-[2-(piperidin-1-yl)ethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1243 | +++++ | 4-Chloro-N-(2-fluoro-5-chlorophenyl)-N-[2-[[[pyrrolidin-1-yl]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1244 | +++++ | 4-Chloro-N-(2-fluoro-5-chlorophenyl)-N-[2-[[N'-[3-(1H-imidazol-1-yl)propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1245 | +++++ | 4-Chloro-N-(2-fluoro-5-chlorophenyl)-N-[2-[[N'-[2-(1H-imidazol-4-yl)ethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1246 | +++++ | 4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[N'-[3-(1H-imidazol-1-yl)propylamino]carbonyl]oxy]-(1R)-(2R)-dimethylethyl]benzenesulfonamide |
| 1247 | +++++ | 4-Chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-[3-(1H-imidazol-1-yl)propyl]-N'-ethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |

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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|---|
| 1248 | +++++ | 4-Chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-[3-(1H-tetrazol-1-yl)-propylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1249 | +++++ | 4-Chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-[2-(hydroxyethyl)-N'-methylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1250 | +++++ | 4-Chloro-N-(2,5-dichlorophenyl)-N-[2-[[N'-[3-(1H-imidazol-1-yl)propyl]-N'-methylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1251 | +++++ | 4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[N'-[3-(1H-imidazol-1-yl)propyl]-N'-cyclopropylmethylamino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1252 | +++++ | 4-Chloro-N-[5-chloro-2-(hydroxymethyl)phenyl]-N-[2-[[N'-[3-(1H-imidazol-1-yl)propyl]-N'-(2-methylethyl)amino]carbonyl]oxy]-(R)-1-methylethyl]benzenesulfonamide |
| 1253 | ++ | 4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-[1-[2-(methylsulfonyl)ethyl] pyrrolidin-2-yl]ethyl]benzenesulfonamide |
| 1254 | + | 4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-pyrrolidin-2-yl]ethyl]benzene sulfonamide |
| 1255 | + | 4-chloro-N-(2,5-dichlorophenyl)-N-[1-(S)-[1-[(1,1-dimethylethoxy) carbonyl]pyrrolidin-2-yl]ethyl]benzenesulfonamide |
| 1256 | ++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-4-oxobutyl]benzenesulfonamide |
| 1257 | +++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[4-[N-(S)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-4-oxobutyl]benzenesulfonamide |
| 1258 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide |
| 1259 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(carboxy)-3-methylbutyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide |
| 1260 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide |
| 1261 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide |
| 1262 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(carboxy)-2-methylpropyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide |
| 1263 | ++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[6-[N-(S)-[1-(carboxy)-3-methylbutyl]amino]-1-methyl-6-oxohexyl]benzenesulfonamide |
| 1264 | ++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide |
| 1265 | +++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide |
| 1266 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(methoxycarbonyl)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide |
| 1267 | ++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(methoxycarbonyl)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide |
| 1268 | ++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(carboxy)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide |
| 1269 | ++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(S)-[1-(carboxy)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide |
| 1270 | ++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(carboxy)-2-methylpropyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide |
| 1271 | +++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[5-[N-(R)-[1-(carboxy)-3-methylbutyl]amino]-1-methyl-5-oxopentyl]benzenesulfonamide |
| 1272 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[1-methyl-6-(1,1-dioxo-2-methyl-4-thiomorpholinyl)-6-oxohexyl]benzenesulfonamide |
| 1273 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[1-methyl-6-(1,1-dioxo-3-methyl-4-thiomorpholinyl)-6-oxohexyl]benzenesulfonamide |
| 1274 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[1-methyl-6-(1,1-dioxido-2-methyl-4-thiomorpholinyl)hexyl]benzenesulfonamide |
| 1275 | +++++ | (R)-4-Chloro-N-(5-chloro-2-fluorophenyl)-N-[1-methyl-6-(1,1-dioxido-3-methyl-4-thiomorpholinyl)hexyl]benzenesulfonamide |
| 1276 | +++++ | (R)-4-Chloro-N-(2,5-difluorophenyl)-N-[1-[4-fluoro-2-[1-(2-methyl-4-thiomorpholinyl)butanoyl]phenyl]ethyl]benzenesulfonamide |

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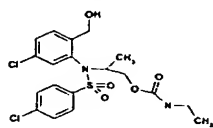
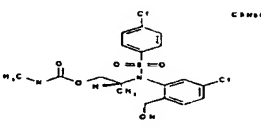
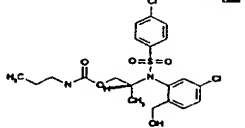
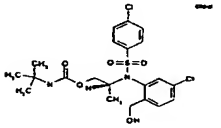
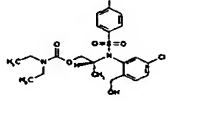
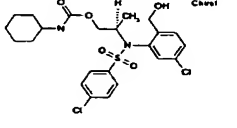
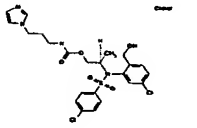
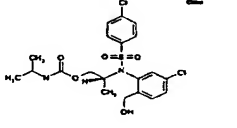
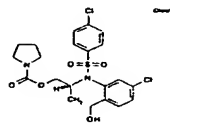
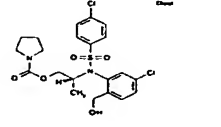
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| NUMBER | ACTIVITY | COMPOUND |
|--------|----------|--|
| 1277 | +++++ | (R)-4-Chloro-N-(2,5-difluorophenyl)-N-[1-[4-fluoro-2-[1-(1,1-dioxo-2-methyl-4-thiomorpholinyl)butanoyl]phenyl]ethyl]benzenesulfonamide |
| 1278 | +++++ | (R)-4-Chloro-N-(2,5-difluorophenyl)-N-[1-[4-fluoro-2-[1-(1,1-dioxo-2-methyl-4-thiomorpholinyl)butyl]phenyl]ethyl]benzenesulfonamide |

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| NUMBER | COMPOUND | ACTIVITY |
|--------|---|----------|
| 1279 |  | +++++ |
| 1280 |  | +++++ |
| 1281 |  | +++++ |
| 1282 |  | +++++ |
| 1283 |  | +++++ |
| 1284 |  | +++++ |
| 1285 |  | +++++ |
| 1286 |  | +++++ |
| 1287 |  | +++++ |
| 1288 |  | +++++ |

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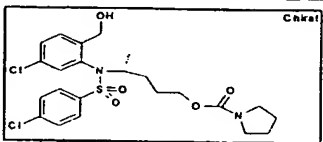
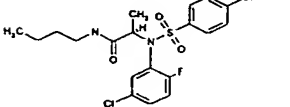
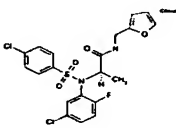
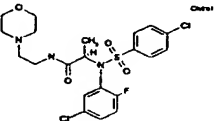
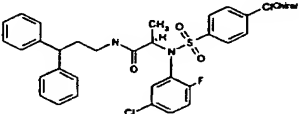
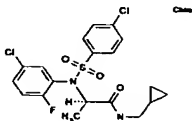
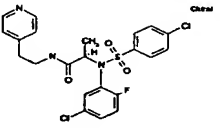
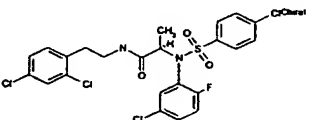
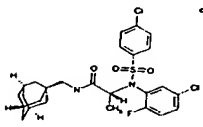
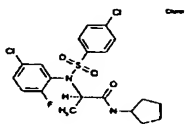
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| NUMBER | COMPOUND | ACTIVITY |
|--------|------------|----------|
| 1289 | Chem 1 | +++++ |
| 1290 | Chem 2 | + |
| 1291 | Chem 3 | +++++ |
| 1292 | Chem 4 | - |
| 1293 | Chem 5 | - |
| 1294 | Chem 6 | +++++ |
| 1295 | Chem 7 | +++++ |
| 1296 | Chem 8 | - |
| 1297 | Chem 9 | +++++ |

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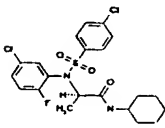
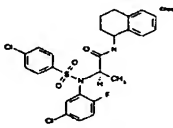
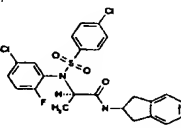
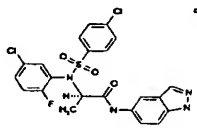
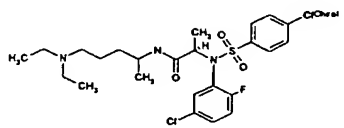
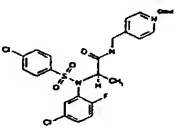
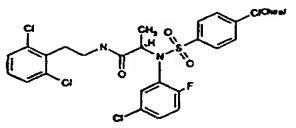
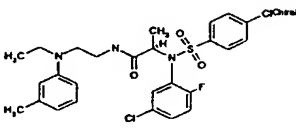
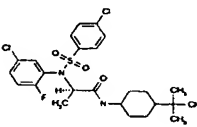
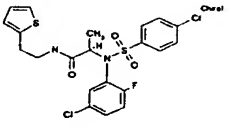
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| NUMBER | COMPOUND | ACTIVITY |
|--------|---|----------|
| 1298 |  | +++++ |
| 1299 |  | ++ |
| 1300 |  | ++ |
| 1301 |  | + |
| 1302 |  | + |
| 1303 |  | ++ |
| 1304 |  | ++ |
| 1305 |  | + |
| 1306 |  | + |
| 1307 |  | ++ |

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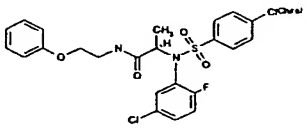
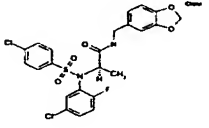
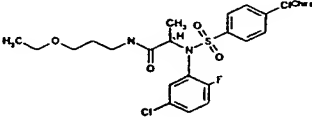
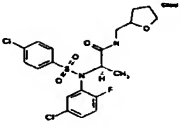
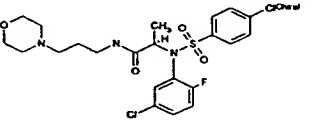
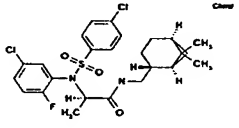
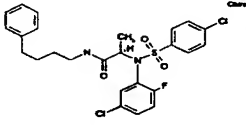
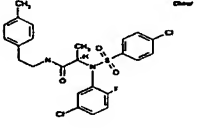
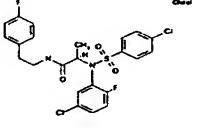
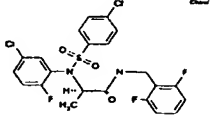
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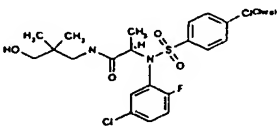
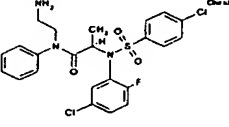
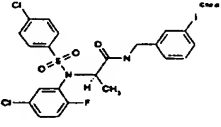
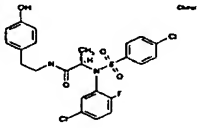
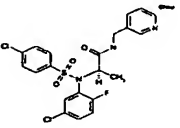
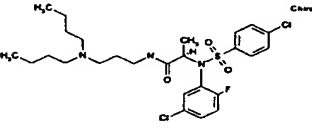
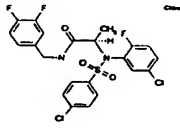
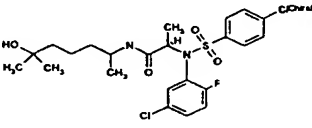
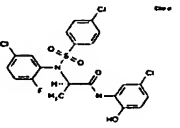
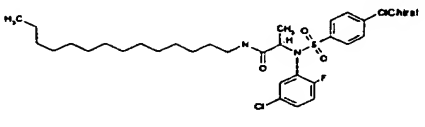
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| 1311 |  | + |
| 1312 |  | + |
| 1313 |  | ++ |
| 1314 |  | ++ |
| 1315 |  | + |
| 1316 |  | + |
| 1317 |  | + |

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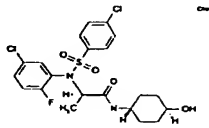
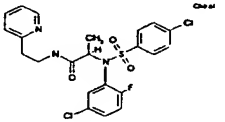
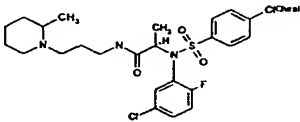
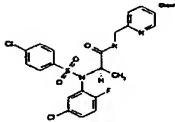
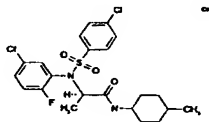
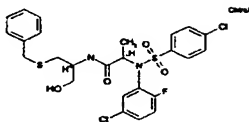
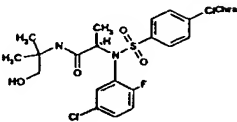
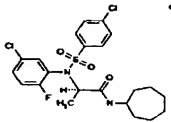
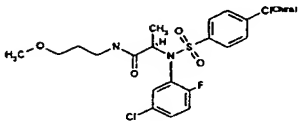
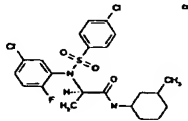
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| 1322 |  | + |
| 1323 |  | + |
| 1324 |  | + |
| 1325 |  | + |
| 1326 |  | + |
| 1327 |  | + |

| NUMBER | COMPOUND | ACTIVITY |
|--------|---|----------|
| 1328 |  | ++ |
| 1329 |  | + |
| 1330 |  | + |
| 1331 |  | + |
| 1332 |  | ++ |
| 1333 |  | + |
| 1334 |  | + |
| 1335 |  | + |
| 1336 |  | + |
| 1337 |  | + |

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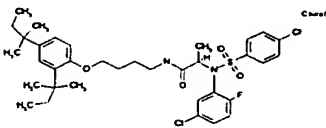
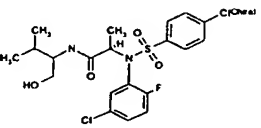
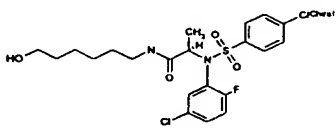
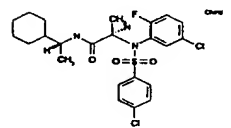
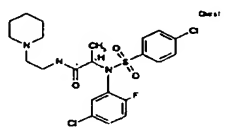
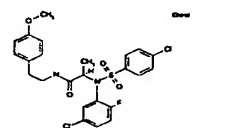
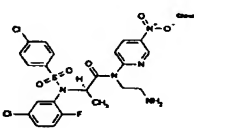
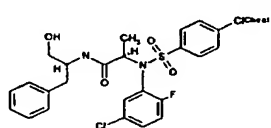
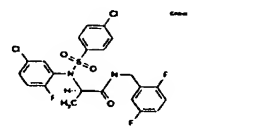
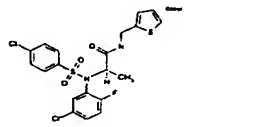
PCT/US00/04560

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| 1340 |  | + |
| 1341 |  | ++ |
| 1342 |  | ++ |
| 1343 |  | + |
| 1344 |  | ++ |
| 1345 |  | ++ |
| 1346 |  | ++ |
| 1347 |  | ++ |

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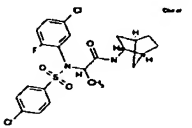
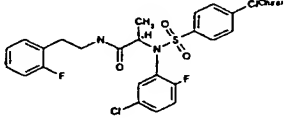
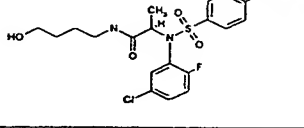
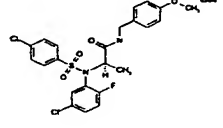
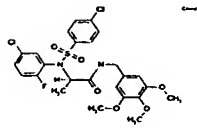
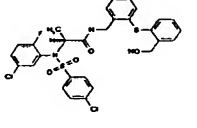
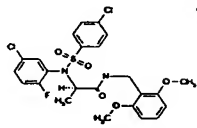
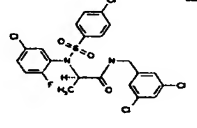
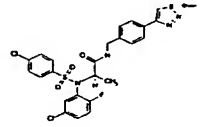
PCT/US00/04560

| NUMBER | COMPOUND | ACTIVITY |
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| 1352 |  | + |
| 1353 |  | + |
| 1354 |  | + |
| 1355 |  | + |
| 1356 |  | + |
| 1357 |  | ++ |

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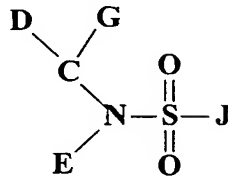
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| 1362 |  | + |
| 1363 |  | + |
| 1364 |  | + |
| 1365 |  | + |
| 1366 |  | + |

Inspection of the extensive dates presented in the preceding Table reveals that a wide variety of compounds of the generic formula provided herein display activity in an *in vitro* cell-based assay.

- 5 While the invention has been described in detail with reference to certain preferred embodiments thereof, it will be understood that modifications and variations are within the spirit and scope of that which is described and claimed.

WHAT IS CLAIMED IS:

1. A compound having the structure:



- 5 and pharmaceutically acceptable salts thereof, wherein:

D is hydrogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, halogen, alkoxy, ester, amide, or

D and G, taken together, form a substituted or unsubstituted cyclic moiety; and

- 10 E, is hydrogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, alkoxy, amide, sulfonyl, sulfonamidyl, sulfide or alkoxy; or

J and E, taken together, form a substituted or unsubstituted cyclic moiety; and

- 15 G, when not part of a cyclic moiety including D, is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted heterocycle optionally having one or more double bonds, amine, amide, ester, ether or carbamate; or

J, when not part of a cyclic moiety including E, is substituted or unsubstituted hydrocarbyl, heterocycle optionally having one or more double bonds.

2. The compound of claim 1, wherein:

- 20 D is H or lower alkyl;
E, G and J are independently substituted or unsubstituted aromatic.

3. The compound of claim 1, wherein:

- 25 E, G and J are independently substituted or unsubstituted 5-, 6- or 7-membered aromatic.

4. The compound of claim 3, wherein:

E, G and J are independently substituted or unsubstituted aryl.

5. The compound of claim 4 wherein:

substituent(s) on E is(are) independently substituted or unsubstituted alkyl, halogen, hydroxy, ester, -S-alkyl, NO₂ or SO₂;

- 5 substituent(s) on G is(are) independently substituted or unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, halogen, amide, amine, hydroxy, sulfonyl, sulfonamide, -(CH₂)_n-O-(CH₂)_m-amine, -(CH₂)_n-O-(CH₂)_m-heterocycle, or -(CH₂)_n-O-(CH₂)_m-amide,

wherein n and m are independently 0, 1, 2, 3, 4 or 5; and

- 10 substituent(s) on J is (are) independently substituted or unsubstituted alkyl, halogen, ether, -S-alkyl, or -S-aryl.

6. The compound of claim 5, wherein:

substituent(s) on E and J is (are) halogen; and

substituent(s) on G is (are) halogen and/or substituted alkyl.

15

7. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted aryl;

G is substituted or unsubstituted aryl; and

20

J is substituted or unsubstituted polycyclic radical.

8. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted aryl;

25

G is substituted or unsubstituted aryl; and

J is substituted or unsubstituted alkyl, alkenyl or alkynyl.

9. The compound of claim 1, wherein:

D is H or lower alkyl;

30

E is substituted or unsubstituted aryl;

G is substituted or unsubstituted aryl; and

J is substituted or unsubstituted heterocycle optionally having or more double bonds.

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10. The compound of claim 1, wherein:

D is H or lower alkyl;

G is substituted or unsubstituted aryl;

E and J, taken together, form a substituted or unsubstituted bicyclic or polycyclic moiety.

11. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted alkyl, alkenyl, or alkynyl;

G is substituted or unsubstituted aryl; and

J is substituted or unsubstituted aryl.

12. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted cycloalkyl, cycloalkenyl, or cycloalkynyl;

G is substituted or unsubstituted aryl; and

J is substituted or unsubstituted aryl.

13. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted polycyclic radical;

G is substituted or unsubstituted aryl; and

J is substituted or unsubstituted aryl.

14. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted heterocycle optionally having one or more double bonds;

G is substituted or unsubstituted aryl; and

J is substituted or unsubstituted aryl.

15. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted aryl;

G is substituted or unsubstituted alkyl, alkenyl and alkynyl; and

J is substituted or unsubstituted aryl.

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16. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted aryl;

G is substituted or unsubstituted cycloalkyl, cycloalkenyl or cycloalkynyl;

J is substituted or unsubstituted aryl.

17. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted aryl;

G is ester or carboxylate;

J is substituted or unsubstituted aryl.

18. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted aryl;

J is substituted or unsubstituted aryl; and

G is substituted or unsubstituted polycyclic radical.

19. The compound of claim 1, wherein:

D is H or lower alkyl;

E is substituted or unsubstituted aryl;

G is $-(CHR_1)_n-O-(CHR_2)_m-CONR_3R_4$, wherein

n is 1, 2, 3 or 4;

m is 0, 1, 2, 3 or 4;

R₁ and R₂ are independently H, or substituted or unsubstituted alkyl;

R₃ and R₄ are independently H, substituted or unsubstituted alkyl;

or R₃ and R₄ cooperate to form a substituted or unsubstituted cyclic moiety; and

J is substituted or unsubstituted aryl.

20. A composition comprising a compound according to claim 1 in a pharmaceutically acceptable carrier therefor.

21. A method of modulating the level of Amyloid Beta Precursor Protein (APP), said method comprising contacting said protein with at least one compound according to claim 1.

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22. A method according to claim 21, wherein said APP is APP₇₅₁, APP_{695wt}, APP_{670/671}, APP_{670/671/717}, sAPP, α -sAPP, or β -sAPP.

23. A method for treating disease conditions, said method comprising administering to a patient having a disease condition a therapeutically effective amount of at least one compound according to claim 1.

24. A method according to claim 23, wherein said disease condition is amyloid angiopathy, cerebral amyloid angiopathy, systemic amyloidosis, an Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis of the Dutch type, inclusion body myositis, and Down's syndrome.

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25. A method for preventing disease conditions in a subject at risk thereof, said method comprising administering to said subject a therapeutically effective amount of at least one compound according to claim 1.

10 26. A method for treating a subject in need thereof to decrease production of A β , said method comprising administering to said subject an effective amount of the compound according to claim 1.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/04560

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C311/21 C07C323/41 C07D211/24 C07D311/20 C07D207/08
C07D277/06 C07D295/12 A61K31/18 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BEILSTEIN Data, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | WO 98 03166 A (MONSANTO) 29 January 1998 (1998-01-29) page 3, line 36 -page 4, line 13 --- | 1-21,23, 25,26 |
| X | WO 98 22104 A (G. PASINETTI, ET AL.) 28 May 1998 (1998-05-28) the whole document --- | 1-21,23, 25,26 |
| A | US 5 624 937 A (J.K. REEL, ET AL.) 29 April 1997 (1997-04-29) the whole document --- | 1,20,21, 23,25,26 |
| P,X | US 5 981 168 A (P.B. REINER, ET AL.) 9 November 1999 (1999-11-09) the whole document ----- | 1-21,23, 25,26 |

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

29 June 2000

Date of mailing of the international search report

06/07/2000

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

English, R

International Application No. PCT/US 00 04560

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-20 (partially)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search with respect to Claims 1-20 has been restricted to compounds listed in example 636, i.e. compounds containing the partial structure, 4-Cl-C₆H₄-SO₂N(CHMe-R)-Ar, where Ar is 2,5-difluorophenyl, 2,5-dichlorophenyl or 5-chloro-2-hydroxymethylphenyl; and R is any group falling within the definition of G given in Claim 1.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/04560

| Patent document cited in search report | | Publication date | Patent family member(s) | | Publication date |
|---|---|---------------------|----------------------------|---|---------------------|
| WO 9803166 | A | 29-01-1998 | AU 3890397 | A | 10-02-1998 |
| | | | CN 1238688 | A | 15-12-1999 |
| | | | CZ 9900168 | A | 11-08-1999 |
| | | | EP 0939629 | A | 08-09-1999 |
| | | | NO 990247 | A | 19-03-1999 |
| | | | PL 331338 | A | 05-07-1999 |
| WO 9822104 | A | 28-05-1998 | US 5985930 | A | 16-11-1999 |
| | | | AU 5361298 | A | 10-06-1998 |
| | | | EP 0956009 | A | 17-11-1999 |
| | | | NO 992374 | A | 21-07-1999 |
| US 5624937 | A | 29-04-1997 | NONE | | |
| US 5981168 | A | 09-11-1999 | AU 3991999 | A | 06-12-1999 |
| | | | WO 9959597 | A | 25-11-1999 |

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